

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: Serguei SOUKHAREV et al.
 Title: FLUORESCENT SUBSTRATES FOR DETECTING
 ORGANOPHOSPHATASE ENZYME ACTIVITY
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PETITION TO MAKE SPECIAL UNDER 37 C.F.R. § 1.102(d)

Mail Stop Petition
 Commissioner for Patents
 P.O. Box 1450
 Alexandria, VA 22313-1450

Sir:

Applicants hereby petition the Patent and Trademark Office under 37 C.F.R. § 1.102(d) and MPEP § 708.02(XI) to make special the instant application. A check in the amount of \$130.00 for the required fee pursuant to 37 C.F.R. § 1.17(h) is attached. This petition is submitted on the grounds that the present invention provides a valuable tool in the fight against terrorism.

**Statement According To MPEP § 708.02(XI) Explaining
 How The Invention Contributes To Countering Terrorism**

The risk of a terrorist attack in the form of the clandestine release of a chemical agent, such as a nerve agent, poses a significant threat.¹ Indeed, the nerve agent sarin has already been used in a terrorist attack against the Tokyo subway system, resulting in a dozen deaths and

¹ See CRS Report for Congress: *Small-scale Terrorist Attacks Using Chemical and Biological Agents: An Assessment Framework and Preliminary Comparisons* (May 20, 2004) (Exhibit A).

injuries to thousands of others.² Moreover, it is believed that Al-Qa'ida and other extremist groups currently have access to these types of agents.³ The release of a nerve agent could cause significant loss of human life and wide-spread fear and panic, as demonstrated in the Tokyo subway attack.

One particular class of nerve agents is organophosphate nerve agents. These agents include tabun, sarin, soman, GF, and VX. These types of nerve agents are inhibitors of acetylcholinesterase (AChE) and can cause death within minutes.⁴ Accordingly, tools for dealing with organophosphate nerve agents are valuable tools in our counter-terrorism arsenal.⁵

One of the obstacles in dealing with a chemical agent attack is detecting the agents released. For example, it would be extremely useful to check areas during decontamination for any remaining chemical agents or to check for remaining chemical agents during patient treatment. Thus, tools are desired that quickly and accurately detect and identify even minute quantities of chemical agents. These tools can minimize the extent of an attack and assist in diagnosis and treatment to maximize the prospect of recovery.

The present invention provides a system that can be used for detecting organophosphate nerve agents. Organophosphatases, such as paraoxonase, bind to and break down organophosphates, such as organophosphate nerve agents. The present invention provides fluorescent substrates for detecting organophosphatases, such as paraoxonase. Spec. ¶ [0002]. Thus, the substrates of the present invention can be used to detect organophosphate nerve agents, as discussed in the specification. See Spec. ¶ [0003], [0016]-[0018] & [0066]. For example, organophosphate nerve agents can be detected “through the specific inhibition of substrate induced fluorescence.” Spec. ¶ [0016]; *see also* ¶ [0066]. Accordingly, the present invention

² See BBC News: *Sarin Attack Remembered in Tokyo* (March 20, 2005) (Exhibit B).

³ See *Terrorist CBRN: Materials and Effects*, available at, http://www.cia.gov/cia/reports/terrorist_cbrn/terrorist_CBRN.htm (Exhibit C).

⁴ See CDC Chemical Emergencies: *Nerve Agents and Organophosphate Pesticides* (March 28, 2005) (Exhibit D).

⁵ See BBC News: *Push for anti-nerve agent drug* (May 2, 2004) (Exhibit E).

can be used to detect organophosphate nerve agents and to minimize the impact of organophosphate nerve agent attack.

Treating victims of chemical attacks and protecting first responders also poses a challenge in countering terrorism. Indeed, treatment options are limited, and first responders are often delayed in providing treatment by the risk of becoming victims by rushing to the scene unprotected. Accordingly, treatment and prevention of poisoning are a top priority in countering the risk posed by chemical attacks.

The present invention provides a system for identifying compounds, proteins in particular, that can be used to treat and/or protect against organophosphatase nerve agents. Specifically, the present invention provides substrates that are highly sensitive and specific for organophosphatases. *See e.g.*, Spec. ¶ [0012]. Thus, the present invention could be used to identify new organophosphatases for breaking down organophosphate nerve agents. In fact, an existing organophosphatase has already been investigated for decontamination and prevention of the effects of organophosphate nerve agents in exposed individuals. *See* Exhibit E. The present invention could further this endeavor by providing a means to identify additional organophosphatases that could be used for decontamination, treatment, and prophylaxis. Thus, the present invention provides a tool that can be used to find new compounds for treating victims and protecting first responders of organophosphate nerve agent attacks.

Conclusion

Applicants believe they have satisfied all of the requirements for this patent application to be granted special status. Granting this petition is earnestly solicited.

Respectfully submitted,

Date 20 October 2005

By Stephen A. Bent

FOLEY & LARDNER LLP

Customer Number: 22428

Telephone: (202) 672-5404

Facsimile: (202) 672-5399

Stephen A. Bent

Attorney for Applicants

Registration No. 29,768

Fubst A

CRS Report for Congress

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Small-scale Terrorist Attacks Using Chemical and Biological Agents: An Assessment Framework and Preliminary Comparisons

May 20, 2004

Dana A. Shea
Analyst in Science and Technology Policy
Resources, Science, and Industry Division

Frank Gottron
Analyst in Science and Technology Policy
Resources, Science, and Industry Division

Small-scale Terrorist Attacks Using Biological and Chemical Agents: An Assessment Framework and Preliminary Comparisons

Summary

This report, which will be updated as necessary, presents a means of assessing the relative threat from terrorist-use of individual chemical, biological, and toxin agents. It focuses on small-scale, targeted chemical and biological attacks, rather than mass-casualty attacks. The framework considers the elements of access, public health impact, medical treatment, prophylaxis, and dissemination. Other factors that may affect potential use by terrorists include the range of lethality, covert employment of an agent, and the availability of dual-use technologies.

The results of this framework may be useful in addressing the threat these agents pose, for example by indicating priorities for countermeasure funding. Other uses include weighing the potential effectiveness of policy options, assessing threat reduction approaches to specific agents, and serving as a resource for developing other specialized frameworks.

Defense against chemical and biological agents is high on the list of the nation's priorities. No clear consensus exists with respect to which agents pose the greatest threat. Previous analyses of the chemical and biological threat have largely revolved around historical and comparative treatments or been based in a military framework. Examination of the chemical and biological threat to civilians is more complicated. Agents whose characteristics make them poor military weapons may still be powerful if deployed as weapons of terror. Chemical and biological weapons used in the past have not always been chosen for the highest potential fatalities, but rather for other reasons.

Some chemical and biological agents are closely regulated, both domestically and internationally. Expansion or further refinement of policies controlling these agents may lower the threat posed by terrorist use of them. Domestic policy options to reduce the threat posed by these agents include methods to prevent their use, consequence management after their use, and methods for protecting the public from them. Specific policies to implement these goals include improving the general public health system, increasing prophylaxis research, development of new medical countermeasures treatments, increasing intelligence gathering, and increasing regulation of dual-use technology. International policy options include development of new biosecurity agreements and increasing participation in current non-proliferation organizations.

It is impossible to eliminate the risk of chemical or biological terrorism. Important issues facing policymakers include balancing the need for increased security with the potential economic costs associated with increased regulation and redirected federal resources, determining the relative ratio between general and specific countermeasures against chemical and biological terrorism, and assessing the success of federal efforts at reducing chemical and biological terrorism vulnerability.

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Small-scale Terrorist Attacks Using Biological and Chemical Agents: An Assessment Framework and Preliminary Comparisons

Introduction

Public concern about the nation's vulnerability to chemical and biological (C/B) terrorism was amplified by the consequences of the anthrax mailings that sickened 22 people and killed 5 between September and November, 2001. Subsequent C/B terrorism events, such as the ricin mailings to the White House in 2003 and to the Senate in 2004, have served to highlight the potential for future terrorist attacks using C/B agents. C/B weapons, previously considered to be of interest mainly to military planners, are now a topic of public and congressional interest. Compared with most conventional weapons, C/B weapons are less well understood and have the potential to cause mass casualties. Even if used in smaller attacks, C/B weapons have the potential to cause mass terror. Potential effects of a C/B terrorist event vary widely, depending on the agent used, the effectiveness of its dissemination, the target struck, and the public reaction to the event.

This report addresses the potential terrorist use of C/B agents, including toxins. The focus of this report is on small-scale, targeted chemical and biological attacks. In this framework, manufacture and dissemination of modest amounts of material, able to cause significant casualties in a building, subway station or other enclosed space, rather than on a citywide scale, are discussed. This approach attempts to analyze the threat posed by various agents if used by small, non-state-sponsored terrorist groups that may lack the technology, expertise, or logistical capability to mount a large mass-casualty attack. To provide policymakers with background and analysis for prioritization of federal resources, this framework summarizes the characteristics of each agent into broad categories with a coarse scale, rather than a highly differentiated, multidimensional ranking. It is likely that policymakers will find more detailed analysis than that presented here helpful when refining policy alternatives.

Reports that discuss chemical and biological agents must be careful not to provide terrorist groups with information or opportunities that are not already known to them. This report follows the precedent set by other publications in this field by not providing detailed information on the C/B agents discussed herein.¹ It does not

¹ Publications in the C/B arena include Richard A. Falkenrath, Robert D. Newman and Bradley A. Thayer, *America's Achilles' Heel: Nuclear, Biological, and Chemical Terrorism and Covert Attack*, Cambridge, MA: MIT Press, 1998; Joshua Lederberg, ed., *Biological* (continued...)

contain any technical information regarding the growth or synthesis of biological or chemical agents. Furthermore, all information in this report has been compiled solely from reports in the open literature. No classified information was used in the preparation of this report. It raises issues expressed by other analysts in disparate open sources with regard to current terrorist motivational factors. The material in this report is designed to be used as a potential springboard to assess and prioritize responses to the various C/B agents that might be used by a terrorist. It provides a potential policy framework for use by Congress as it considers legislative issues associated with the potential use of such agents by terrorists.

Some previous assessments of the C/B threat have highlighted the difficulty of developing and producing agents, but these assessments may ignore significant advances in the areas of dual-use technology.² Such technology may significantly ease C/B agent production by small groups. Additionally, concerns have been raised about the applicability of previous assessments, especially those developed using a military framework, to civilian settings and casualties. The classification of C/B weaponry into the catch-all category of “weapons of mass destruction” (WMD) has led to consideration of C/B use primarily on a mass-casualty scale.³ This treatment may misstate the potential civilian vulnerability to a small-scale terrorist C/B attack. Treatment of terrorist attacks on a mass-casualty scale has produced many worst-case scenarios, but few assessments of the wide spectrum of potential C/B agents.

The merging of all unconventional, high-consequence/low-probability-of-use weapons into a single category is advantageous for some military planning, but can obfuscate assessment of each weapon type or individual agent. All of the weapons of mass destruction differ from each other significantly in effect, effort required for development, and production and dissemination. While the impact of nuclear and radiological devices varies largely depending on the size of the device, the impact of different chemical and biological agents has wider variation. For example, the agent used can determine if the result is temporary impairment, injury and disfigurement,

¹ (...continued)

Weapons: Limiting the Threat, Cambridge, MA: MIT Press, 1999; Bill Frist, *When Every Moment Counts: What You Need to Know About Terrorism By The Senate's Only Doctor*, Lanham, MD: Rowman & Littlefield, 2002; National Research Council, *Making the Nation Safer: The Role of Science and Technology in Countering Terrorism*, Washington, DC: National Academies Press, 2002; and *Microbial Threats to Health: Emergence, Detection, and Response*, Institute of Medicine, Washington, DC: National Academies Press, 2004.

² Dual-use technologies have a legitimate civilian use in addition to a military use.

³ This assessment method has been ubiquitous in both governmental and private-sector assessments. As examples, see the White House Fact Sheet, *Combating Terrorism: Presidential Decision Directive 62*, May 22, 1998; Centers for Disease Control and Prevention, “Biological and Chemical Terrorism: Strategic Plan for Preparedness and Response: Recommendations of the CDC Strategic Planning Workgroup,” *Morbidity and Mortality Weekly Report* 49 RR-4 (2000): 2-3; Jonathan B. Tucker and Amy Sands, “An Unlikely Threat,” *Bulletin of the Atomic Scientists* 55 (July-August 1999): 46-52; and World Health Organization, *Health Aspects of Chemical and Biological Weapons*, Geneva: World Health Organization, 1970, 98-99.

or widespread death. This report treats C/B agents alone, rather than assessing WMD, to better address the threat posed by individual C/B agents.

Addressing events with small-scale casualties generally has been outside the purview of previous assessments, though small-scale terrorism is noted as being more likely than mass-casualty events.⁴ After the events of October 2001, small-scale terror events also concern the public. It is a concern for policymakers that analyses on, and preparations against, large-scale chemical and biological attacks may not be widely applicable to events occurring on smaller scales. This concern was expressed in the first annual report of the Advisory Panel to Assess the Domestic Response Capabilities of the Government for Terrorism Involving Weapons of Mass Destruction, also known as the Gilmore Commission. Looking at lower probability/higher consequence scenarios, it stated:

Such scenarios, however, are at odds with the focus of current policy and preparedness efforts — which have been based on less than comprehensive information and analysis — which seem to emphasize the lower-probability/higher-consequence attacks at the expense of higher-probability/lower-consequence incidents. The guiding assumption has been that smaller-scale, non-mass-casualty events are a lesser-included contingency that can be addressed adequately by preparations for the higher-end mass casualty attacks. This is by no means axiomatic.⁵

To address these concerns, this report focuses on smaller-scale, targeted terror attacks, rather than addressing C/B weapons in a mass-casualty framework.

This report establishes an assessment framework for C/B agents to help policymakers develop risk-management based policies to counter terrorist use of C/B agents. Vulnerability, threat, and risk are related terms. Vulnerability represents the impact an event could have, and contains measures of protection and preparedness. Threat represents the probability that a given event will occur, and contains measures of both capability and intention. Risk is the combination of vulnerability with threat. Risk management approaches rely on reducing vulnerability, threat, or both to lower the overall risk of attack. The assessment framework presented here is generic in the sense that it does not incorporate the motivations or capability of a specific terrorist organization. A risk assessment of a specific terrorist organization's likelihood of using C/B weapons would incorporate these factors.

Independent think tanks and federal government agencies have developed and modeled scenarios, through exercises including federal and local officials, to assess the potential impact of a C/B attack. These exercises provide vulnerability assessment rather than threat or risk assessment. The potential public threat posed

⁴ See The Advisory Panel to Assess the Domestic Response Capabilities of the Government for Terrorism Involving Weapons of Mass Destruction, "The First Annual Report to the President and the Congress of The Advisory Panel to Assess the Domestic Response Capabilities of the Government for Terrorism Involving Weapons of Mass Destruction: I. Assessing the Threat," Dec. 15, 1999, available on-line from RAND at [<http://www.rand.org/organization/nsrd/terrpanel>].

⁵ *Ibid.*

by C/B terrorism is not accurately assessed through the development of worst-case scenario exercises such as Dark Winter, TOPOFF, TOPOFF 2 and others.^{6,7} These exercises are instructive in establishing the United States' current C/B vulnerability, but they do not assess many factors needed to understand the C/B risk. For example, it is unclear whether the pathogens chosen for the exercises (smallpox and pneumonic plague, respectively) represent agents likely to be chosen by a terrorist. Without understanding the range of *likely* C/B agents, rather than the range of *possible* C/B agents, it is difficult to convert vulnerability assessments into threat assessments. Therefore, it is difficult to make effective policy based strictly on vulnerability assessments. The General Accounting Office (GAO) has advocated using a risk-management approach, rather than vulnerability assessments, to limit the potential damage done by a C/B attack.⁸

Background

Definition of C/B Terrorism

There are several federal definitions of terrorism.⁹ For example, the U.S. Department of Defense (DOD) defines terrorism as "The calculated use of unlawful violence or threat of unlawful violence to inculcate fear; intended to coerce or to intimidate governments or societies in the pursuit of goals that are generally political,

⁶ The Johns Hopkins Center for Civilian Biodefense Strategies, in collaboration with the Center for Strategic and International Studies, the Analytic Services Institute for Homeland Security, and the Oklahoma National Memorial Institute for the Prevention of Terrorism, held a senior-level exercise in June, 2001 entitled "Dark Winter" that simulated a covert smallpox attack on the United States. A review of the Dark Winter exercise can be found in Tara O'Toole, Michael Mair, and Thomas V. Inglesby, "Shining Light on "Dark Winter," *Clinical Infectious Diseases* 34 (2002): 972-983.

⁷ The U.S. Department of Justice conducted an exercise, called TOPOFF for its involvement of *top officials*, in May 2000, regarding the management of mock radiological, chemical, and biological attacks in three cities. A review of the TOPOFF 2000 exercise can be found in Thomas V. Inglesby, Rita Grossman, and Tara O'Toole, "A Plague on Your City: Observations from TOPOFF," *Clinical Infectious Diseases* 32 (2001): 436-445. In May 2003, the U.S. Department of Homeland Security conducted TOPOFF 2 to test the response to a radiological and biological terrorist attack. See U.S. Government, *Top Officials (TOPOFF) Exercise Series: TOPOFF 2, After Action Summary*, U.S. Department of Homeland Security, Washington DC, December 19, 2003.

⁸ The GAO has often cited the need for a risk management approach to chemical and biological terrorism in both testimony before and reports to Congress. For representative examples, see testimony by Raymond J. Decker before the Senate Committee on Governmental Affairs. General Accounting Office, *Homeland Security: A Risk Management Approach Can Guide Preparedness Efforts*, GAO-02-208T, October 2001, and General Accounting Office, *Bioterrorism: Coordination and Preparedness*, GAO-02-129T, October 2001.

⁹ For an overview of the statutory language defining terrorism, see CRS Report RS21021 "Terrorism" and Related Terms in Statute and Regulation: Selected Language by Elizabeth Martin.

religious, or ideological.”¹⁰ The U.S. Department of Justice (DOJ) defines terrorism as “...the unlawful use of force and violence against persons or property to intimidate or coerce a government, the civilian population, or any segment thereof, in furtherance of political or social objectives.”¹¹ Because of differences in federal definitions of terrorism, especially in the areas of threatened use and articulation of goals, this report uses a more encompassing definition for C/B terrorism. For the purposes of this report, C/B terrorism refers to the use of chemical or biological agents by individuals or groups motivated by ideology, but not necessarily accompanied by a stated political or social agenda.¹² By using this definition, attacks which have a large apparently random component to them may be included as terrorist events.¹³ This definition includes several C/B terrorist events to date, such as the ricin mailings in 2003 and 2004, the anthrax mailings in 2001, the Aum Shinrikyo sarin gas attack in Tokyo in 1995,¹⁴ and the Rajneeshees’ use of salmonella poisoning in Oregon in 1984.¹⁵

Probability of a C/B Weapon Attack

Most experts agree that the probability of a C/B attack on a domestic target remains much smaller than that of a comparably damaging attack with conventional arms. The instantaneous consequence of, greater access to, and relative ease of using conventional weapons all contribute to the likelihood of conventional weapon use. Additionally, terrorist organizations have historically chosen to use proven attack methods, rather than attempt attacks with less well-established technologies.¹⁶ Experts debate whether C/B agents have become weapons with special value to potential terrorists due to their psychological effect on the public. Some experts have

¹⁰ U.S. Department of Defense, “DOD Dictionary of Military and Associated Terms,” *Joint Publication 1-02*, as amended through December 17, 2003.

¹¹ 28 C.F.R. 0.85, also see U.S. Department of Justice, *Terrorism in the United States*, Federal Bureau of Investigation, 1999.

¹² The definition used here closely follows that used by W. Seth Carus in *Bioterrorism and Biocrimes: The Illicit Use of Biological Agents Since 1900*, Center for Counterproliferation Research, Washington, DC: National Defense University, 2001.

¹³ This definition is not the broadest definition for terrorism, as it excludes actions taken by nation-states and does not require that the victims of terrorism be noncombatants.

¹⁴ For an overview of the Aum Shinrikyo use of sarin in the Tokyo subway system, see David E. Kaplan, “Aum Shinrikyo (1995)” in *Toxic Terror: Assessing Terrorist Use of Chemical and Biological Weapons*, ed. Jonathan B. Tucker, Cambridge, MA, MIT Press, 2000.

¹⁵ For an overview of the Rajneeshees’ use of *Salmonella* Typhimurium in Oregon in 1984, see W. Seth Carus, “The Rajneeshees (1984)” in *Toxic Terror: Assessing Terrorist Use of Chemical and Biological Weapons*, *op. cit.*

¹⁶ See, for example, Bruce Hoffman, “Holy Terror,” *the Implications of Terrorism Motivated by a Religious Imperative*, RAND Document P-7834, 1993.

asserted that terrorist groups will continue to escalate the level of violence employed, including C/B agents, so that reaction and attention is drawn to their actions.¹⁷

Some experts feel that it is simply a matter of time until terrorists begin using C/B weapons in earnest. In a 1999 *Washington Post* opinion article, then Defense Secretary Cohen stated:

Also looming is the chance that these terror weapons will find their way into the hands of individuals and independent groups — fanatical terrorists and religious zealots beyond our borders, brooding loners and self-proclaimed apocalyptic prophets at home. This is not hyperbole. It is reality.¹⁸

In May, 2002, Defense Secretary Rumsfeld told the Senate Appropriations Committee, “... they [terrorists] inevitably will get their hands on them [weapons of mass destruction] and they will not hesitate to use them.”¹⁹ Experts holding this view believe it is a matter of “when” rather than “if” terrorists will use C/B or other WMD technology against civilian targets.

Other experts believe that the historical record shows few successful attempts at C/B terrorism, and that past trends will be equally applicable to the future. For example, Milton Leitenberg, a senior fellow at the Center for International and Security Studies at the University of Maryland, has written “...the threat assessment, most particularly regarding “BW terrorism” — the potential for BW use by non-state actors — has been greatly exaggerated.”²⁰

Some experts claim that the ease of using conventional weapons so heavily outweighs the potential benefits of using a more challenging, unconventional method that it makes C/B terrorism unlikely. Anthony H. Cordesman, Arleigh A. Burke Chair in Strategy at the Center for Strategic and International Studies, stated “Most terrorist/extremist attacks to date on Americans inside and outside the U.S. have used conventional explosives, and the [1993] World Trade Center and Oklahoma City bombings show that such attacks can be very costly.”²¹

The public’s response to highly visible acts of property destruction may provide a disincentive for C/B agent usage. Groups accustomed to shocking the populace

¹⁷ See, for example, Jeffrey D. Simon, “The Growing Threat of Bioterrorism”, in *The Age of Super and Cyber Terrorism. Selected Papers* (Arlington, VA: Potomac Institute for Policy Studies) 1999.

¹⁸ William S. Cohen, “Preparing for a Grave New World,” *The Washington Post*, July 26, 1999.

¹⁹ “Rumsfeld Says Terrorists Inevitably Will Get Chemical, Nuclear or Biological Weapons,” *Associated Press*, May 21, 2002. Bracketed information added by CRS.

²⁰ Milton Leitenberg, “Biological Weapons and ‘Bioterrorism’ in the First Years of the 21st Century,” Center for International and Security Studies, April 3, 2003. Found online at [<http://www.fas.org/bwc/papers/21centurybw.pdf>].

²¹ Anthony H. Cordesman, “Defending America: Asymmetric and Terrorist Attacks with Biological Weapons,” Center for Strategic and International Studies, February 12, 2001.

through infrastructure destruction may choose to use conventional weapons rather than unconventional arms because of the greater visual display of property destruction. Also, C/B agent development requires greater time and financial investment than development of conventional explosives, and it demands a higher degree of training. Groups may not be able or willing to invest such a high proportion of resources in unconventional weapons given the relative ease of obtaining and using conventional weapons. Finally, the effects of C/B agents are more unpredictable than conventional weapons and may be delayed in time. This uncertainty may make them less likely to be chosen by a terrorist group, especially a group with limited resources or opportunity.²²

In contrast, some analysts point out that the changing nature of terrorist organizations may lower the barriers for those groups who wish to use chemical or biological agents.²³ Historically, terrorist groups tended to possess clear, defined political aims and easily identified constituents. These groups' activities were constrained by the cultural and moral beliefs of their constituents, including the general aversion to the use of chemical or biological agents. Additionally, the potential for disease transmission from an infected terrorist target to a terrorist supporter was viewed as a barrier to biological terrorism. Recently, terrorist groups bearing a fundamentalist, extremist view lacking clear political goals and having a diffuse, less easily identified constituency have become more common. Many analysts suspect that the taboo against use of C/B agents has weakened, since these groups may be less susceptible to traditional deterrents and may be less concerned with maintaining a high level of legitimacy to their constituents. Changes in political makeup of these groups also may result in a reassessment of the terrorists' choice between conventional and unconventional arms.²⁴

Recent advances in dual-use technology may reduce the technological barriers for terrorist groups who wish to engage in C/B-related attacks. Industries and academia, especially in the area of microbiology, increasingly employ technologies that can be converted to C/B agent production with moderate to low effort. These dual-use technologies provide prospective terrorists with equipment that can be obtained by theft or purchase. Policymakers may be required to reassess the likelihood of terrorists using C/B agents, as technical barriers to C/B agent development may become less of a hindrance.²⁵

²² Another possibility is the use of chemical or biological agents in conjunction with conventional weapons. The combination of these two attack types presents additional policy challenges and considerations which are beyond the scope of this report.

²³ For an overview of the different factors potentially motivating terrorist groups towards C/B use, see Jerrold M. Post, "Psychological and Motivational Factors in Terrorist Decision-Making: Implications for CBW Terrorism" in *Toxic Terror: Assessing Terrorist Use of Chemical and Biological Weapons*, *op. cit.*

²⁴ For an in-depth examination of this issue see, CRS Report RL31831 *Terrorist Motivations for Chemical and Biological Weapons Use: Placing the Threat in Context* by Audrey Kurth Cronin.

²⁵ For more on this topic, see CRS Report RS21422 *Dual-Use Biological Equipment: Difficulties in Domestic Regulation* by Dana A. Shea.

Historical Acquisition and Use of C/B Agents

Many chemical and biological agents have been used in the past, both during times of war and through terrorist action. The former Soviet Union and the United States both possessed active chemical and biological weapons programs that attempted to develop new, more deadly weapons.²⁶ Currently, international treaties restrict research to that for defensive purposes only. Other nations have, at various times, also developed their own biological and chemical programs, though some of these programs are no longer supported.²⁷

Chemical and biological weapons were initially developed in a military context, as weapons with potential strategic and tactical use. Chemical agents were widely used in Europe during World War I, and biological agents were reportedly used in sabotage actions against animals in World War I.²⁸ Also, Japan has been cited as using plague as an antipersonnel weapon against China during World War II.²⁹ The former Soviet Union has been accused of providing toxin agents to allies in Vietnam and Laos and using these toxins during its war in Afghanistan.³⁰ During the 1980-1988 Iraq-Iran war, both Iran and Iraq reportedly used chemical agents, with both countries using vesicants and Iraq purportedly employing nerve agents.³¹ It has also been widely reported that Iraq used chemical agents against Kurdish civilians to quell an insurgency.³²

²⁶ The Russian Federation and the United States have ratified the Chemical Weapon Convention which went into force in 1997. On November 25, 1969, President Nixon ended the U.S. offensive biological weapons program. The former Soviet Union's offensive biological weapons program persisted into at least the 1990's; an account of which is in Ken Alibek's *Biohazard: The Chilling True Story of the Largest Covert Biological Weapons Program in the World — Told from Inside by the Man Who Ran It*, New York: Random House, 1999.

²⁷ For an overview of the historical development and wartime use of C/B agents, see Javed Ali, Leslie Rodrigues and Michael Moodie, *U.S. Chemical-Biological Defense Guidebook*, Alexandria, VA: Jane's Information Group, 1998. For more information regarding national weapons programs, see CRS Report RL30699 *Nuclear, Biological, and Chemical Weapons and Missiles: The Current Situation and Trends*, by Sharon Squassoni and *Chemical and Biological Weapons: Possession and Programs Past and Present*, Monterey Institute for International Studies, found online at [<http://cns.miiis.edu/research/cbw/possess.htm>].

²⁸ W. Seth Carus, *Bioterrorism and Biocrimes: The Illicit Use of Biological Agents Since 1900*, *op. cit.*

²⁹ See "Chronology of State Use and Biological and Chemical Weapons Control" compiled by Center for Nonproliferation Studies, Monterey Institute of International Studies, updated: October, 2001, found online at [<http://cns.miiis.edu/research/cbw/pastuse.htm>].

³⁰ Jonathan B. Tucker, "The 'Yellow Rain' Controversy: Lessons for Arms Control Compliance," *The Nonproliferation Review*, Spring, 2001.

³¹ Julian Perry Robinson and Jozef Goldblat, *Chemical Warfare in the Iraq-Iran War*, Stockholm International Peace Research Institute, May 1984.

³² For example see, Staff Report, U.S. Congress, Senate, Committee on Foreign Relations, *Chemical Weapons Use in Kurdistan: Iraq's Final Offensive*, 100th Congress, 2nd session, (continued...)

Some terrorist groups have adopted C/B agents to further their aims. In 1984, the Rajneeshees sickened hundreds of people in Oregon by producing and deploying *Salmonella* Typhimurium, a bacterium which normally causes non-fatal food poisoning.³³ Aum Shinrikyo developed an array of chemical and biological agents to be used against the Japanese civilian populace in the early 1990s.³⁴ There are also many reports of small groups or individuals producing toxin agents.³⁵ While it is difficult to determine the extent to which terrorist groups are researching potential chemical and biological weapon use, it has been reported that some known terrorist groups have an interest in acquiring such weapons.³⁶

C/B Assessments

Assessments by Government Agencies. An assessment of terrorist threat is difficult to quantify, since many of the variables involved are not reliably known. Some of these variables include the skill level of various terrorist groups, the location and size of terrorist assets, and the possession of any particular C/B agent. As a consequence, the exact threat faced is indeterminable from the open literature and the risk involved can only be estimated. Vulnerability can be assessed through the development of scenarios, including worst-case scenarios. Vulnerability studies do not address the likelihood of an attack occurring; they only assess possible outcomes if an attack very similar to the one modeled occurs. It is commonly thought that a worst-case scenario is unlikely to occur, since many low-probability events must occur for the worst to happen. However, given the nature of some C/B agents, even non-worst-case events could have huge psychological effects, public health impacts and economic costs for the nation.

With few historical precedents for C/B terrorism, determining the current risk of C/B terrorism from past events is difficult and perhaps misleading. To assess the threat from other nations, the U.S. intelligence community has prepared several National Intelligence Estimates on the biological and chemical capabilities of foreign states.³⁷ Within these classified estimates, reportedly, the C/B agents that have the

³² (...continued)

U.S. Government Printing Office, 1988.

³³ W. Seth Carus, "The Rajneeshees" in *Toxic Terror: Assessing Terrorist Use of Chemical and Biological Weapons*, *op. cit.*

³⁴ David Kaplan, "Aum Shinrikyo" in *Toxic Terror: Assessing Terrorist Use of Chemical and Biological Weapons*, *op. cit.*

³⁵ For an extensive overview of the use of chemical, biological, and toxin agents by non-state actors see Ron Purver, *Chemical and Biological Terrorism: The Threat According to the Open Literature*, Canadian Security Intelligence Service, 1995. A comprehensive compilation of biological agent use and its context can be found in W. Seth Carus, *Bioterrorism and Biocrimes: The Illicit Use of Biological Agents Since 1900*, *op. cit.*

³⁶ Central Intelligence Agency, *Unclassified Report to Congress on the Acquisition of Technology Relating to Weapons of Mass Destruction and Advanced Conventional Munitions, 1 January Through 30 June 2003*, November 2003.

³⁷ A National Intelligence Estimate is the most authoritative written judgment concerning
(continued...)

highest relative probability of use have been described, but these reports are not available in the open literature.³⁸ Presumably, the Directorate for Information Analysis and Infrastructure Protection in the Department of Homeland Security and the Terrorist Threat Integration Center have developed or are in the process of developing similar C/B threat assessments.³⁹

Several other federal agencies have developed, or are in the process of developing, biological agent threat lists, to determine the agents which have the highest relative probability of use.⁴⁰ The Centers for Disease Control and Prevention (CDC), in collaboration with law enforcement, intelligence and defense agencies, have developed a list of agents that would have the greatest impact on the public health.⁴¹ The U.S. Department of Agriculture has developed two biological threat lists through a collaborative, international process.⁴² The Environmental Protection Agency, under provisions of the Clean Air Act, has collected worst-case scenario plans and information regarding catastrophic toxic releases from chemical plants adjacent to or within communities.⁴³ As each agency has different requirements and perspectives, each has generated individualized C/B threat lists. There is a lack of consensus on the contents of a definitive, unified C/B threat list.

Military-use Assessment Compared to Terrorist-use Assessment.

Military-use analyses predominantly revolve around military management of C/B weapons and battlefield casualties. These analyses may inadequately address terrorist use of C/B agents against civilian populations. Several key factors cited as necessary conditions for military use would not be required in a smaller-scale assault on civilian targets using limited dispersal of C/B agents. For example, military assessments include factors such as stabilization of the C/B agent for storage and

³⁷ (...continued)

a national security issue by the major agencies comprising the U.S. intelligence community. Most National Intelligence Estimates forecast future developments and many address their implications for the United States. National Intelligence Estimates cover a wide range of issues including military, technological, economic, and political trends. They are prepared by the Director of Central Intelligence with the participation of intelligence community agencies. See General Accounting Office, *Combating Terrorism: Need for Comprehensive Threat and Risk Assessments of Chemical and Biological Attacks*, GAO/NSIAD-99-163, September, 1999.

³⁸ The accuracy of some NIEs have been questioned. For example, see John Barry and Mark Hosenball, "What Went Wrong," *Newsweek*, February 9, 2004, 24-31.

³⁹ For more on these entities, see CRS Report RS21283 *Homeland Security: Intelligence Support* by Richard A. Best, Jr.

⁴⁰ As cited by General Accounting Office, *Bioterrorism: Coordination and Preparedness*, GAO-02-129T, October 2001, 10.

⁴¹ Lisa D. Rotz, *et al.*, "Public Health Assessment of Potential Biological Terrorism Agents," *Emerging Infectious Diseases* 8 (2002): 225-230.

⁴² As cited by General Accounting Office, *Bioterrorism: Coordination and Preparedness*, GAO-02-129T, October 2001.

⁴³ More information on the Risk Management Program of the EPA can be found online at [<http://yosemite.epa.gov/oswer/CeppoWeb.nsf/content/index.html>].

transport purposes, dispersal technologies for maximum airborne dissemination, timeliness of agent effectiveness, and integration within the battle plan. Additionally, many of the military assessments, especially those relating to chemical agents, are made specifically in relation to use by an opposing military, with considerations of chemical prophylaxis and protective equipment being included. Finally, a recurring theme in military assessments is the difficulties involved in disseminating an agent against a target in the open, a tactic requiring training in meteorology and engineering in addition to chemical and/or biological training.

Concerns of storage, stability and mass dissemination are examples of why a military assessment may differ from one using a terrorism framework. While it is likely true that only a state-funded biological or chemical weapons program could successfully develop the technology necessary to make bulk C/B agents that are stable under long-term storage in munition form, a terrorist who wishes to make gram quantities of a C/B agent and disseminate it, for example with a modified pesticide sprayer, would be unconstrained by these criteria. This underscores the Gilmore Commission's concern that large-scale WMD analysis may be inappropriate when applied to terrorist events.⁴⁴ Agents whose characteristics make them poor military weapons may still be powerful if deployed as weapons of terror.

How Difficult Is it to Develop C/B Agents for Terrorist Use? Experts disagree on the difficulty of C/B agent manufacture. Many experts believe that it is relatively easy to manufacture some chemical agents,⁴⁵ while others point to the apparent difficulties that state actors have had in developing chemical weapons programs. Some experts claim that development of weaponized biological agents presents remarkably high hurdles, particularly in mass dissemination, which would require teams of scientists with state backing to overcome.⁴⁶ Other experts believe that a single, moderately well funded individual could develop a biological weapon in a home basement.⁴⁷ Richard Danzig, while he was Under Secretary of the Navy, stated the opinion that, "[A] small pharmaceutical industry or even moderately sophisticated university or medical research laboratory can generate a significant offensive capability."⁴⁸ Some experts reportedly claim that very pure, high quality anthrax spores similar to those used in the anthrax mailings could be made with "a

⁴⁴ Some terrorist-use assessments of biological weapon use focus significantly on mass casualty threats. See, for example, Centers for Disease Control and Prevention, "Public Health Assessment of Potential Biological Terrorism Agents," *Emerging Infectious Diseases* 8 (2002): 225.

⁴⁵ For a representative opinion, see Robert K. Mullen, "Mass Destruction and Terrorism," *Journal of International Affairs* 32 (1978): 62-89.

⁴⁶ For a representative opinion, see Milton Leitenberg, "An Assessment of the Biological Weapons Threat to the United States," *Conference on Emerging Threats Assessment: Biological Terrorism*, Dartmouth College, July, 2000, found online at [<http://www.homelanddefense.org/journal/Articles/Leitenberg.htm>].

⁴⁷ For a representative opinion, see Jeffrey D. Simon, "Terrorists and the Potential Use of Biological Weapons: A Discussion of Possibilities," RAND Corporation, December 1989.

⁴⁸ See Richard Danzig, "Biological Warfare: A Nation at Risk - A Time to Act," *Strategic Forum*, Institute for National Strategic Studies, January 1996.

very simple, nonindustrial process — a very primitive process — that could let you get a trillion spores in one gram.”⁴⁹ Other experts dispute this assertion.⁵⁰

One explanation for some of the differences among expert views lies in assumptions of event size. Experts who opine that terrorist use of biological and chemical weapons is difficult tend to consider such agents in the framework of mass destruction, with fatalities numbering in the thousands and casualties in the tens of thousands of people, which would require mass production of agents and the independent development of efficient, effective distribution systems.⁵¹ In contrast, others argue that the small batches required for a targeted, low-casualty attack would be relatively easy to produce. The Aum Shinrikyo sarin gas attack in Tokyo and the anthrax mailings demonstrated that an attack utilizing either a chemical or biological agent need not inflict mass casualties to cause widespread disruption.

Figure 1 provides a comparison between the steps necessary to develop a mass-casualty chemical weapon and those required for the same agent to be used on a smaller scale in a terrorist attack. **Figure 2** shows a similar comparison for biological weapons. While the exact criteria needed to develop a C/B agent vary with the agent, the primary difference between the two flowcharts is that for terrorist distribution of a C/B agent, many steps considered to have high practical difficulties may be nonexistent in the case of terrorist groups that wish to launch only a small-scale attack and that have low regard for their personal safety.⁵² Such steps include developing agents that have a long storage shelf life, optimizing a large-scale dissemination device, developing rigorous prophylaxis, and optimizing the manufacturing process so as to make mass quantities of the C/B agent. These steps, indicated by italics in the flowchart for military use, are not necessarily required for terrorist group use and therefore have been removed from the flowchart for terrorist programs.

Experts contend that for large scale attacks these steps represent barriers of comparable importance to a terrorist organization. If terrorist groups focus on smaller scale distribution of C/B agents, the amount of agent necessary to inflict

⁴⁹ Ken Alibek quoted by Jonathan Rauch, “Does Al Qaeda Have Anthrax? Better Assume So,” *National Journal*, May 31, 2002.

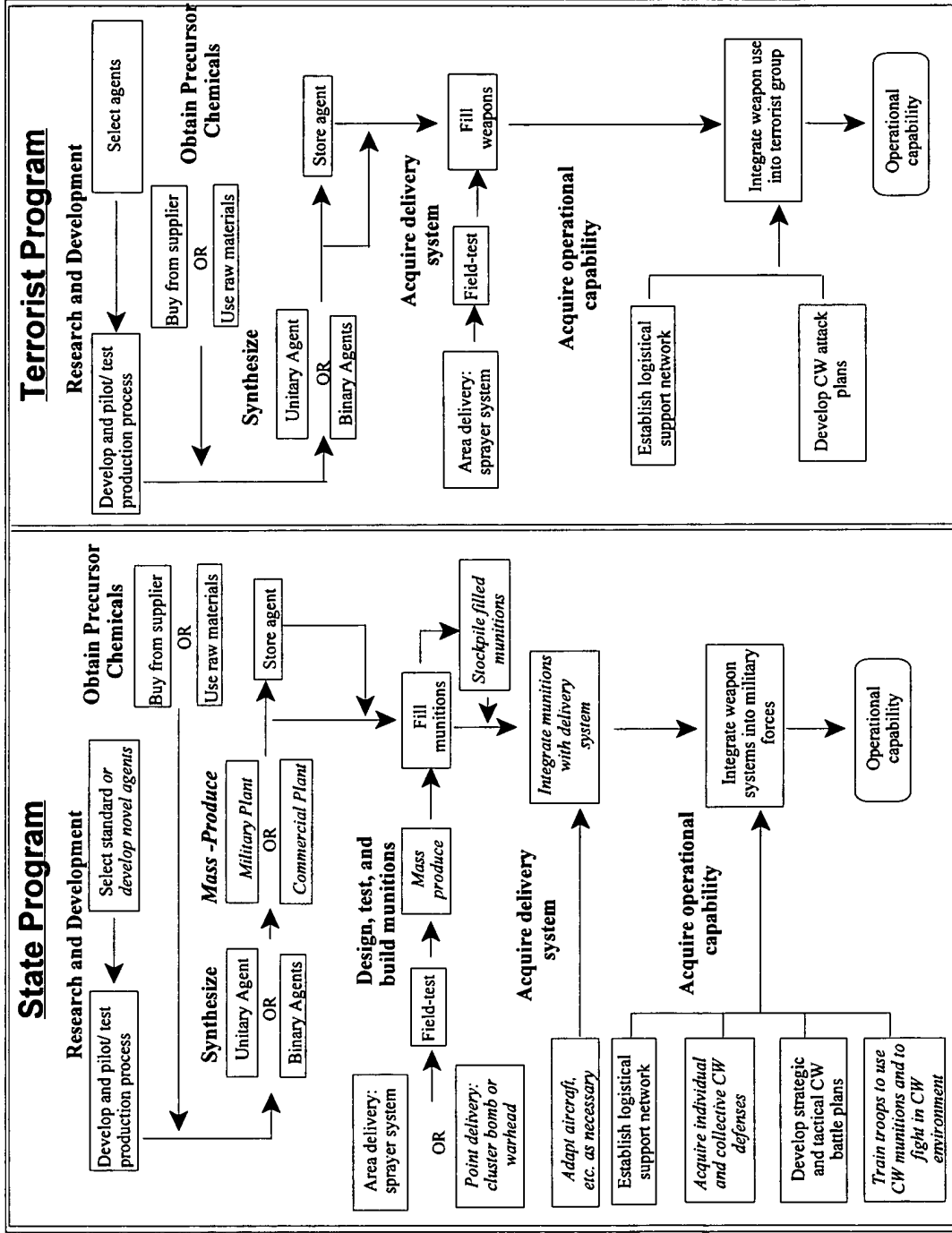
⁵⁰ Gary Matsumoto, “Anthrax Powder: State of the Art?” *Science* 302 (2003): 1492-1497.

⁵¹ The Office of Technology Assessment produced several comprehensive analyses of chemical and biological agents in terms of mass destruction. While dated, the majority of the information contained in these reports continues to be applicable. See U.S. Congress, Office of Technology Assessment, *Technologies Underlying Weapons of Mass Destruction*, OTA-BP-ISC-115, Washington, DC: Government Printing Office, 1993; U.S. Congress, Office of Technology Assessment, *Proliferation of Weapons of Mass Destruction: Assessing the Risks*, OTA-ISC-559, Washington, DC: Government Printing Office, 1993; U.S. Congress, Office of Technology Assessment, *Technology Against Terrorism: Structuring Security*, OTA-ISC-511, Washington, DC: Government Printing Office, 1992; and U.S. Congress, Office of Technology Assessment *Technology Against Terrorism: The Federal Effort*, OTA-ISC-487, Washington, DC: Government Printing Office, 1991.

⁵² For an overview of motivations leading to terrorist use of suicide tactics, see CRS Report RL32058 *Terrorists and Suicide Attacks* by Audrey Kurth Cronin.

dozens to thousands of casualties can be made using only research-scale, rather than mass-production, facilities. If a terrorist group decides that small-scale distribution is acceptable, disseminating agents either as a crude aerosol or solution through the use of converted industrial equipment would become a viable, if inefficient, distribution method. The problem of long-term agent storage is bypassed if only enough material for each use is prepared shortly before being used. These compromises reduce the effective lethality of a given amount of agent, as several non-optimized steps are involved, but this could be addressed through production of more agent. These compromises result in removing many of the hurdles cited as being of maximal difficulty in nation-state-level C/B development.

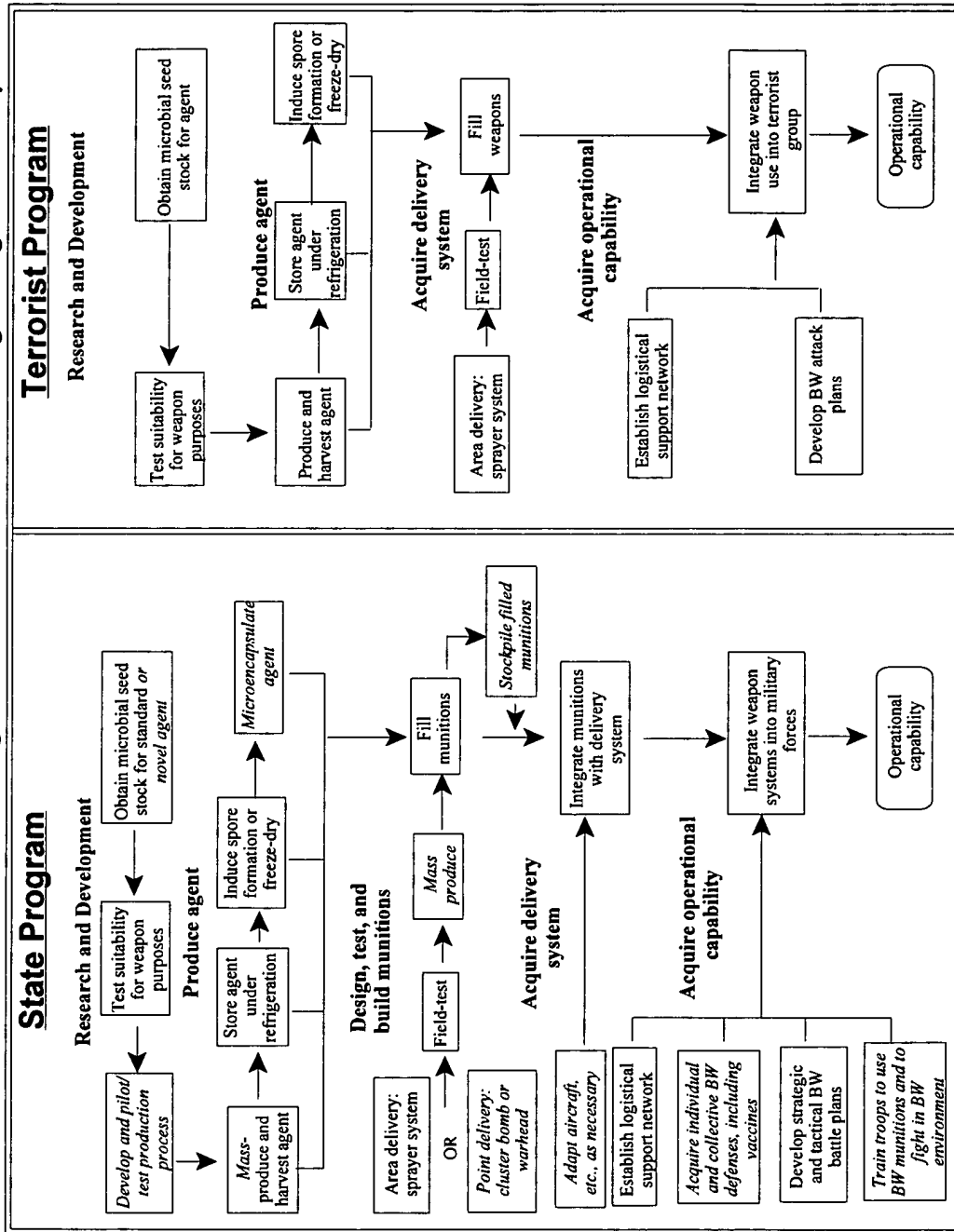
Figure 1. Comparison of State Chemical WMD and Terrorist Chemical Agent Development



Source: Adapted by CRS, 2002 from *Technologies Underlying Weapons of Mass Destruction*, Office of Technology Assessment, December, 1993.

Note: The process required for a nation-state level capability is found on the left, that for a terrorist capability is found on the right. Italics reflect differences between programs.

Figure 2. Comparison of State Biological WMD and Terrorist Biological Agent Development



Source: Adapted by CRS, 2002 from *Technologies Underlying Weapons of Mass Destruction*, Office of Technology Assessment, December, 1993.

Note: The process required for a nation-state level capability is found on the left, that for a terrorist capability is found on the right. Italics reflect differences between programs.

Agent Analysis

C/B agents are presented in a matrix framework in this section, with the agents ranked by number of barriers to their use in small scale terrorist attacks, rather than use in mass-casualty attacks or military use. Because of the differences among the agents, they are divided into three categories: chemical agents, biological agents, and toxins. Toxins are separated from biological agents because they do not reproduce in a host, and are separated from chemical agents because of their biological origin. Each C/B agent type is analyzed according to criteria specific to its category. A negative sign (—) denotes an aspect that poses a significant barrier to terrorist use or that is a negative influence to terrorist use. A positive sign (+) refers to an aspect that does not pose a significant barrier to terrorist use or that is a positive influence to terrorist use. The **O** rank represents an intermediate state. The matrices present agents for comparison within a category, but agents should not be compared across different matrices, as the criteria used vary for each matrix. **Appendix A** contains a detailed description of the methodology used to develop these matrices.

The successful development of a C/B agent requires a certain level of individual competence and training.⁵³ The analysis here applies only to cases where terrorist groups possess such levels of skill. Also, reasonable financial means on the part of the terrorist is assumed. Since this report focuses on the ability of groups or individuals to develop small-scale production capacity, it is also assumed that there is no overt state-sponsorship of the terrorist group, and, as a consequence, there has been no documented technology transfer to the terrorist group from a national biological or chemical weapons program. In order to compare the impact of different C/B agents, the target is assumed to be the same in each case: a medium-sized enclosed space, such as an office building or subway station. The effect of changing these assumptions is explored in the **Discussion** section.

Chemical Agent Comparison

Most chemical agents, unlike biological or toxin agents, do not naturally occur. Typically, a larger amount of chemical agent is required for equivalent effect than a biological or toxin agent. Some chemical agents were discovered during research in chemical warfare and others in civilian research areas, such as pesticide development. Chemical agents have widely varying effects and forms; some chemical agents are toxic or corrosive gases commonly found in industrial processes.⁵⁴ Other chemical agents are not used in manufacturing processes and are used only as a weapon. Finally, some chemical weapons have found civilian applications in other areas and are manufactured for those purposes, for example, nitrogen mustard has been used for cancer chemotherapy.

⁵³ Many experts agree that a graduate education in chemistry or biology provides the necessary skills to produce laboratory quantities of a chemical, biological, or toxin agent respectively. Others believe that some agents might be within the capabilities of intelligent and dedicated high school students.

⁵⁴ Toxic chemicals such as chlorine, phosgene, hydrogen cyanide, and anhydrous ammonia are often used in chemical manufacturing processes.

Choice of Chemical Agents Assessed. There are many toxic chemicals, but most are ill-suited for terrorist use because of their physical properties. The chemical agents discussed in this report are a subset of all available toxic chemicals. Criteria for selecting these agents include their coverage by the Chemical Weapons Convention (CWC),⁵⁵ their inclusion on the CDC's chemical agent list,⁵⁶ their inclusion in North Atlantic Treaty Organization (NATO)⁵⁷ and U.S. military medical fieldbooks,⁵⁸ their inclusion in the U.S. DOJ *Guide for the Selection of Chemical and Biological Decontamination Equipment for Emergency First Responders*,⁵⁹ and finally their reported presence in the former Soviet Union's or the United States' chemical weapons program.⁶⁰ Agents found on a preponderance of these lists were chosen to be included for assessment. Agents with purely psychological effects, such as LSD (lysergic acid diethylamide) or the compound BZ, were omitted.

Criteria. Table 1 categorizes chemical agents according to four criteria: ease of acquisition, public health impact, resistance to medical treatment, and ease of dissemination. Agents are listed in descending order of combined ranking with respect to the criteria. For further information on the methodology regarding criteria choice, ranking, and weighting, see Appendix A. See Table 4 in Appendix B for technical data used to rate each agent.

⁵⁵ The list of chemicals found on the three schedules of the Chemical Weapons Convention can be found online at [http://www.opcw.org/html/db/cwc/eng/cwc_annex_on_chemicals.html].

⁵⁶ The Centers for Disease Control and Prevention list of chemical agents of concern is found at [<http://www.bt.cdc.gov/Agent/AgentlistChem.asp>].

⁵⁷ *NATO Handbook on the Medical Aspects of NBC Defensive Operations AmedP-6(B)*, Departments of the Army, the Navy and the Air Force, 1996, found online at [<http://www.vnh.org/MedAspNBCDef/toc.htm>].

⁵⁸ *Field Manual: Treatment of Chemical Agent Casualties and Conventional Military Chemical Injuries*, Departments of the Army, the Navy, and the Air Force, and Commandant, Marine Corps, July, 2000, found online at [<http://www.vnh.org/FM8285/cover.html>].

⁵⁹ *Guide for the Selection of Chemical and Biological Decontamination Equipment for Emergency First Responders*, NIJ Guide 103 — 00, October, 2001, found online at [<http://www.ncjrs.org/pdffiles1/nij/189724.pdf>].

⁶⁰ Chemical agents found in the former Soviet Union's and the United States' chemical weapons program are taken from a summary developed by the Monterey Institute of International Studies from sources in the open literature. The summary is found online at [<http://cns.miis.edu/research/cbw/possess.htm>].

Table 1. Chemical agent comparison according to barriers to potential terrorist use

Chemical Agent	Ease of Acquisition	Public Health Impact	Resistance to Medical Treatment	Ease of Dissemination
Nitrogen Mustard	+	+	+	+
Sulfur Mustard	+	+	+	+
Phosgene Oxime	O	+	+	+
Lewisite	O	+	O	+
Cyclohexyl Sarin	O	+	O	O
Sarin	O	+	O	O
Tabun	O	+	O	O
VX	—	+	+	+
Ammonia	+	O	+	—
Chlorine	+	O	+	—
Chloropicrin	+	O	+	—
Phosgene	+	O	+	—
Soman	—	+	+	O
Diphosgene	O	O	+	—
Cyanogen Chloride	+	O	—	—
Hydrogen Cyanide	+	O	—	—
Perfluoro-isobutylene	—	O	+	—

Source: This table was prepared from compiled open source data. Congressional Research Service, 2002 (Updated 2004). See **Appendix B** for detailed data used to generate rating.

Note: See text for explanation of symbols. Breaks within the table group agents with roughly comparable rank.

Ease of Acquisition. Most chemical agents require artificial synthesis and manufacture, so a prospective terrorist would be concerned with their relative ease of production. While dual-use chemical agents are potentially available by theft or purchase in large quantity, many chemical agents require a dedicated synthetic effort to acquire in bulk. In some cases, precursor chemicals required to synthesize agents can be purchased on a research scale without undue difficulty.⁶¹

The technology necessary to manufacture most chemical agents is known through the open literature. The safety and efficiency of chemical synthesis and manufacturing practices have increased substantially since the early manufacture of chemical agents. While the equipment necessary for large-scale manufacture of these agents is regulated through export controls, equipment necessary to create small-scale amounts of chemical agents at home, in makeshift laboratory facilities, can be purchased through many chemical distributors. Attempting to manufacture chemical agents under such circumstances comes with increased risk of discovery and inadvertent exposure to the agent.

In the ease of acquisition column of **Table 1**, the symbol + denotes chemical agents that are created via processes that are technically straightforward and have few noxious side products, or those chemicals that have industrial dual-uses and therefore might be obtained rather than manufactured. The symbol O denotes chemical agents that generate significant toxic side products during manufacture, endangering the person manufacturing the agents.⁶² The symbol — denotes chemical agents that require closely monitored precursor chemicals for manufacture, create significant lethal side products, or require sophisticated synthesis equipment.

Public Health Impact. This report combines morbidity, mortality and load placed on the public health care system to describe this aspect of an agent's effectiveness. Effects of a chemical agent are agent-specific. Some agents kill exposed people. Other agents primarily incapacitate victims; these agents, predominantly choking agents, tend to have a wide range of effects, from temporary tightness of chest and difficulty breathing to life-threatening pulmonary edema. Finally, some agents incapacitate those exposed through painful tissue damage. These agents, called blister agents or vesicants, cause damage on contact with the skin and do not need to be inhaled for effect. A single scale of impact, such as lethality, would strongly under-report the impact of a blister agent, which requires relatively large quantities to kill, but little to cause intense pain and disfigurement. On the other hand, using lethality as the only scale would over-report the impact of a nerve agent, which can be lethal, but generally causes much less harm at sub-lethal dosages.

Because of the above factors, this report uses a more general criterion to describe an agent's effectiveness, namely impact on the health care system. Mortality

⁶¹ "Special Report: Better Killing Through Chemistry," *Scientific American*, December, 2001.

⁶² The synthesis of some agents involves the generation of toxic side products. These side products could significantly complicate the production of chemical agents, as they increase the level of danger to the person making the compound.

and morbidity from the release of nerve agent would have a high impact on the health care system, as would cases of extensive chemical burns from the release of blister agents, and cases of pulmonary edema from choking agents. By using this more indirect gauge of effectiveness, useful comparisons can be made between agents with different mechanisms of causing harm.

In the public health impact column of **Table 1**, the symbol + denotes chemical agents whose use would create a high, deleterious public health consequence. The symbol O denotes chemical agents whose use would create a more moderate, deleterious public health consequence. The symbol — denotes chemical agents whose use would create a relatively low, deleterious public health consequence.⁶³

Resistance to Medical Treatment. The degree to which treatment can ameliorate or prevent symptoms is a primary concern in treating chemical casualties. This factor is essential to defusing the impact of a chemical attack. Injuries from some chemical agents cannot be reversed. Injuries from other agents may be successfully reversed through treatment immediately after the attack. Depending on the agent and the quantity of agent to which a victim is exposed, the time frame in which these treatments are effective varies from minutes to hours.⁶⁴

In the resistance to medical treatment column of **Table 1**, the symbol + denotes chemical agents that lack any treatment to prevent the onset of symptoms. The symbol O denotes chemical agents that first responders would likely be able to treat. The symbol — denotes chemical agents which can be treated after a significant time delay.

Ease of Dissemination. Chemical agents are typically dispersed as a gas or liquid, depending on the ambient temperature and the agent. Gases dilute themselves into the surrounding atmosphere, limiting their effectiveness. In most cases, chemical agent effects arise from some form of interaction with the vapors or the aerosols of these agents. Liquids that are not volatile do not provide enough vapor for inhalation and must either be aerosolized or heated to maintain their effect.

In the ease of dissemination column of **Table 1**, the symbol + denotes chemical agents which do not require inhalation to inflict damage, the vapors or aerosol cause an effect upon skin contact. The symbol O denotes chemical agents which require inhalation of small quantities of vapor or aerosol. The symbol — denotes chemical agents that require inhalation of large volumes of vapor or aerosol.

Examples. Chlorine is a chemical commonly used in many manufacturing and industrial processes, ranging from the pharmaceutical industry to water treatment facilities. Because of its wide availability, chlorine receives a + in the ease of

⁶³ No — symbols appear in this column, as chemicals with low public health impact did not pass the selection criteria for inclusion in this framework.

⁶⁴ For information on the aging times of various nerve agents, see Frederick R. Sidell, "Nerve Agents," in *Medical Aspects of Chemical and Biological Warfare*, eds. Frederick R. Sidell, Ernest T. Takafuji, and David R. Franz, Washington, DC: TMM Publications, 1997, 129-179.

acquisition category. Because chlorine can cause serious lung damage but is rarely lethal, chlorine receives a **O** in the public health impact category. These injuries cannot be cured, and can only be treated with supportive care; therefore chlorine receives a + in the resistance to medical treatment category. Finally, for chlorine to cause harm, large volumes of the gas must be inhaled, and therefore chlorine receives a — in the ease of dissemination category.

In contrast to chlorine, the nerve agent VX is much harder to acquire.⁶⁵ There is no industrial use for VX and the known existing sources are under military guard. A terrorist bent on using VX would most likely need to manufacture it from precursor chemicals. However, these chemicals are controlled under the CWC and would not be easy to obtain. Additionally, the synthesis of VX produces highly toxic side products, so VX receives a — for ease of acquisition. VX is deadly at relatively low concentration and many people could be affected by a small-scale attack, therefore VX receives a + in public health impact. Treatment is available for victims of VX exposure, especially those who receive lower doses and prompt attention. However, VX's persistent nature requires first responders to don specialized equipment to enter and treat victims in the contaminated area. This time delay may significantly complicate effective treatment. Therefore, VX receives a + for resistance to medical treatment. Although VX is a liquid at room temperature, it need not be inhaled; skin contact with small quantities is lethal. VX receives a + for ease of dissemination.

The most effective known use of a chemical weapon in a terrorist attack occurred in 1995 when the Aum Shinrikyo cult released sarin into the Tokyo subway. Sarin is not widely available like chlorine gas, but is technically easier to manufacture than VX. It receives a **O** for ease of acquisition. Twelve people died in the attack, more than one thousand were injured, and more than five thousand sought treatment.⁶⁶ Sarin is deadly at relatively low concentration and many people could be affected by a small-scale attack. Therefore, sarin receives a + for public health impact. Treatment is available for victims of sarin exposure, especially those who receive lower doses and prompt attention. Therefore sarin receives a **O** in resistance to medical treatment. Because sarin is a liquid at room temperature and must be inhaled to injure, it receives a **O** for ease of dissemination.⁶⁷ Sarin reportedly was not the original agent of choice for Aum Shinrikyo, as previous attempts were made to develop botulinum toxin and anthrax. The cult apparently developed other chemical agents, such as phosgene and VX, but for various internal political and technical reasons was unable to effectively use these weapons to inflict mass casualties.⁶⁸

⁶⁵ VX is the common name for O-Ethyl S-Diisopropylaminomethyl Methylphosphonothiolate, a toxic nerve agent.

⁶⁶ Tim Ballard *et al.*, "Chronology of Aum Shinrikyo's CBW Activities," Monterey Institute of International Studies, March 15, 2001.

⁶⁷ Liquid sarin can be a deadly upon prolonged skin contact, but its predominant threat is through inhalation of sarin vapor.

⁶⁸ David Kaplan, "Aum Shinrikyo" in *Toxic Terror: Assessing Terrorist Use of Chemical* (continued...)

Biological Agent Comparison

Potential biological agents include the many bacteria and viruses that induce disease in human beings. Many pathogens are not suitable biological agents because of their fragility, long incubation time, or other characteristics. Biological agents differ from chemical agents in that large amounts of agent can be grown from a tiny initial supply. Biological agents may be considered especially insidious compared to other agents, because the pathogens can multiply within infected individuals. Thus, the dosage needed to induce illness can be very low, an amount much smaller by weight than required of chemical or toxin agents.

Choice of Biological Agents Assessed. The biological agents chosen for inclusion in **Table 2** were compiled from several sources including the Biological Weapons Convention (BWC) draft Compliance Protocol Annex A list,⁶⁹ the CDC Select Agent list,⁷⁰ the CDC Biological Diseases/Agents Listing,⁷¹ the *NATO Handbook on the Medical Aspects of NBC Defensive Operations*,⁷² the U.S. DOD *Field Manual: Treatment of Biological Warfare Agent Casualties*,⁷³ the Australia Group List of biological agents for export control,⁷⁴ the World Health Organization's *Preparedness for the Deliberate Use of Biological Agents*,⁷⁵ the U.S. DOJ *An Introduction to Biological Agent Detection Equipment for Emergency First Responders*,⁷⁶ the former Soviet Union's bioweapons program, and the United States' former biological weapons program.⁷⁷ Biological agents found on a preponderance of these lists were selected for assessment.

⁶⁸ (...continued)

and *Biological Weapons*, *op. cit.*

⁶⁹ The rolling text for the draft Biological Weapons Convention Protocol from February, 2001 was used, found online at [<http://www.fas.org/bwc/papers/febannex1.htm#aann>].

⁷⁰ The Select Agent list is defined in 42 C.F.R. 73.4.

⁷¹ The CDC Biological Diseases/Agents Listing can be found online at [<http://www.bt.cdc.gov/Agent/Agentlist.asp>].

⁷² *NATO Handbook on the Medical Aspects of NBC Defensive Operations AmedP-6(B)*, *op. cit.*

⁷³ *Field Manual: Treatment of Biological Warfare Agent Casualties*, *op. cit.*

⁷⁴ The Australia Group List of Biological Agents for Export Control can be found online at [http://www.australiagroup.net/en/control_list/bio_agents.htm].

⁷⁵ World Health Organization, *Preparedness for the Deliberate Use of Biological Agents: A rational approach to the unthinkable*, World Health Organization, Geneva, May, 2002, found online at [http://whqlibdoc.who.int/hq/2002/WHO_CDS_CSR_EPH_2002.16.pdf].

⁷⁶ *An Introduction to Biological Agent Detection Equipment for Emergency First Responders*, NIJ Guide 101-00, December, 2001, found online at [<http://www.ncjrs.org/pdffiles1/nij/190747.pdf>].

⁷⁷ Biological agents found in the former Soviet Union's and United States' former biological weapons program can be found in a summary developed by the Monterey Institute of International Studies from sources in the open literature. The summary is found online at [<http://cns.miiis.edu/research/cbw/possess.htm>].

Criteria. **Table 2** categorizes biological agents based on six criteria: ease of acquisition, public health impact, prophylaxis, resistance to medical treatment, ease of dissemination, and whether the pathogen has been developed for use in a military setting (“weaponized”). Agents are listed in descending order of combined ranking with respect to the criteria. For further information on the methodology regarding criteria choice, ranking, and weighting, see Appendix A. See **Table 5** in **Appendix C** for technical data used to rate each agent.

Ease of Acquisition. In marked contrast to chemical agents, most biological agents can be obtained from natural sources, but natural strains vary widely in their virulence. In some cases, biological agents are endemic in an animal reservoir population, simplifying access and development. This availability provides terrorists with options in developing a self-contained biological agent capacity. Terrorists could attempt to isolate a pathogen found in nature, obtain a sample from a natural human outbreak, or purchase or steal a sample from a commercial culture collection or hospital. This would provide enough source material for a small-scale production facility, using liter-sized fermenters, or even petri dishes, to grow enough material for a small-scale attack.

In assessing the ease of a pathogen’s acquisition, several factors were weighed. The first is whether the biological agent is available in an accessible area. Biological agents which are rare cannot be readily or reasonably obtained from nature and would need to be acquired from preexisting samples. For example, Marburg virus would be very difficult to obtain from nature.⁷⁸ It could be obtained from a culture collection, but such transfers are closely regulated and observed. There would be large practical barriers to their acquisition, regardless of the legality of such a transfer. In contrast, salmonella bacteria would be easy to obtain from natural sources and are available in many culture collections.

In the ease of acquisition column of **Table 2**, the symbol + denotes biological agents that are endemic in nature, have well documented outbreaks, or are routinely disseminated from culture collections. The symbol **O** denotes biological agents that are available in nature only in very localized or remote areas, have small or poorly documented outbreaks, or are obtained primarily through culture banks. The symbol — denotes biological agents that are located predominantly in restricted culture banks and are rarely documented in the wild.

⁷⁸ Marburg virus causes a rare hemorrhagic fever with high lethality. The location of the natural reservoir for Marburg virus is not well established.

Table 2. Biological agent comparison according to barriers to potential terrorist use

Disease (Biological Agent)	Ease of Acquisition	Public Health Impact	Prophylaxis	Resistance to Medical Treatment	Ease of Dissemination	Weaponized
Glanders (<i>Burkholderia mallei</i>)	+	+	+	O	+	Weapon
Crimean-Congo hemorrhagic fever	+	+	+	O	+	Unknown
Pneumonic Plague (<i>Yersinia pestis</i>)	+	+	O	O	+	Weapon
Hantavirus	+	+	+	O	O	Research
Dengue hemorrhagic fever	O	+	O	+	O	Research
Eastern equine encephalitis	O	+	O	+	O	Research
Lassa fever	O	O	+	O	+	Research
Russian spring-summer encephalitis	O	O	O	+	+	Research
Western equine encephalitis	O	O	O	+	O	Research
Rift Valley fever	O	O	O	O	O	Research
Marburg hemorrhagic fever	—	+	+	+	+	Weapon
Ebola hemorrhagic fever	—	+	+	+	+	Research
Melioidosis (<i>Burkholderia pseudomallei</i>)	+	+	+	—	+	Research
Yellow fever	+	+	—	+	+	Research
Anthrax (<i>Bacillus anthracis</i>)	+	+	—	O	+	Weapon
Q fever (<i>Coxiella burnetii</i>)	+	+	O	—	+	Weapon

Disease (Biological Agent)	Ease of Acquisition	Public Health Impact	Prophylaxis	Resistance to Medical Treatment	Ease of Dissemination	Weaponized
Machupo hemorrhagic fever	—	+	+	O	+	Research
Tularemia (<i>Francisella tularensis</i>)	O	+	O	—	+	Weapon
Junin hemorrhagic fever	—	+	O	O	+	Research
Venezuelan equine encephalitis	O	—	O	+	O	Weapon
Typhus (<i>Rickettsia prowazekii</i>)	+	O	O	—	O	Research
Rocky Mountain spotted fever (<i>Rickettsia rickettsiae</i>)	O	+	O	—	O	Unknown
<i>Escherichia coli</i> O157:H7	+	—	+	+	—	Unknown
Smallpox (<i>Variola major</i>)	—	+	—	O	+	Weapon
Monkeypox	—	+	—	O	+	Unknown
Brucellosis (<i>Brucella abortus</i> , <i>B. melitensis</i> , <i>B. suis</i>)	+	—	O	—	+	Research
<i>Shigella dysenteriae</i>	O	+	+	—	—	Unknown
Cholera (<i>Vibrio cholerae</i>)	+	—	—	—	+	Unknown
<i>Salmonella</i> Typhimurium	+	—	+	—	—	Unknown
Typhoid fever (<i>Salmonella</i> Typhi)	+	O	—	—	—	Unknown

Source: This table was prepared from compiled open source data. Congressional Research Service, 2002 (Updated 2004). See Appendix C for detailed data used to generate rating.

Note: See text for explanation of symbols. Breaks within the table group agents with roughly comparable rank.

Public Health Impact. Biological agents, like chemical agents, can induce a range of effects. Some agents are primarily incapacitating in nature, while other agents are acutely lethal.⁷⁹ The public health impact criterion used here is the same as used above for chemical agents.

In the public health impact column of **Table 2**, the symbol + denotes biological agents that have high, deleterious public health impact. The symbol O denotes biological agents that have a more moderate, deleterious public health impact. The symbol — denotes biological agents that have a relatively low, deleterious public health impact.

Prophylaxis. Vaccines and other prophylactic measures are important factors in assessing whether a particular agent would be a useful weapon in either military or terrorist terms. The availability of a vaccine could provide civilian targets with high protection from particular agents if the vaccine is routinely administered. The presence of a widely used vaccine might significantly deter terrorist use of that biological agent.⁸⁰ Biological agents against which the population is routinely vaccinated have been removed from this analysis.⁸¹

In the prophylaxis column of **Table 2**, the symbol + denotes biological agents with no established prophylaxis. The symbol O denotes biological agents with experimental prophylaxis lacking Food and Drug Administration approval. The symbol — denotes biological agents with an approved vaccine.

Resistance to Medical Treatment. There is no uniform medical treatment for biological agents. Some diseases are not curable and can only be treated with generalized supportive care to limit symptoms. Other diseases can be cured through the use of specific medicines. Furthermore, some diseases are treatable at any time in the progression of the illness, while others can only be successfully treated during onset. Treatment potential is likely to be an important consideration for a terrorist. An agent which is easily treated has little offensive utility, while an agent which is not curable might have a high value even if it only leads to an incapacitating disease. Additionally, the chance for self-infection with an incurable pathogen may also factor into the terrorist decision-making process.

In the resistance to medical treatment column of **Table 2**, the symbol + denotes biological agents which have no specific treatment outside of supportive care. The symbol O denotes biological agents which can be treated with agent-specific medicine in a narrow time frame, or have a potential, but unproven, treatment. The symbol — denotes biological agents which can be cured without restriction.

⁷⁹ Incapacitating agents may still result in fatalities depending on the infectious dose, the individual's immune system strength, and other complicating factors.

⁸⁰ The existence of effective prophylaxis may conversely enhance a prospective terrorist's ability to use an agent, if the terrorists place a premium on their own safety. The level of external, mechanical protection required to handle and produce biological agents is decreased when effective prophylaxis is available.

⁸¹ Polio is an example of a disease against which the population is routinely vaccinated. A terrorist attack using this pathogen would likely cause little harm.

Ease of Dissemination. Unlike chemical agents, biological agents can reproduce and are generally grown suspended in liquid solutions. They are more difficult than chemical agents to effectively disseminate in the air. They may be disseminated via other media (see below). Some biological agents can be dried and ground into small particles which can be released as aerosols, but this is a fairly advanced technique. Because of the natural filtering capacity of the human airways, there is an optimal range of particle size that will deeply penetrate the lungs. Many experts cite the difficulty of preparing or disseminating biological agents in such a particle size range as a primary barrier to terrorist use. Other experts counter that commercial dissemination equipment, namely technologies similar to yard foggers and crop dusters, can be adapted to provide aerosols that, while not optimal in size, will still be infectious. Additionally, not all biological agents must be lodged deep in the lungs to cause infection.

Some biological agents are contagious from person to person. Each person infected with a biological agent which is contagious by casual contact can become a new dissemination vector. These highly contagious agents might be viewed by terrorists as more useful than other types of biological agents, as people not in the original exposed area may fall ill through such contact. All other factors being equal, contagious agents that require close contact may be viewed by a terrorist as less useful than those needing only casual contact, due to the lower probability of secondary infection.

Another common infectious pathway is through ingestion via contaminated water, beverages, or food, but some pathogens are less virulent by this route than by inhalation. It is logistically complex to affect large numbers of people with a significantly lethal pathogen through contaminating the food or water supply. Still, as shown by the Rajneeshees' use of *Salmonella* Typhimurium to contaminate restaurant salad bars in Oregon, low-technology approaches, such as food contamination, may be effective.

In the ease of dissemination column of **Table 2**, the symbol + denotes biological agents that are amenable to dissemination as an aerosol and through ingestion, or are contagious through close contact.⁸² The symbol O denotes biological agents that can be disseminated as an aerosol. The symbol — denotes biological agents that require ingestion or dissemination using an animal vector, such as a mosquito, tick, or other insect.

Weaponization. Some biological agents were reportedly developed by either the Soviet Union's or the United States' former biological weapons program. While most of these agents were only research targets, several pathogens were successfully converted into military grade weapons. Due to these research efforts, the knowledge necessary to convert a naturally occurring disease into an optimized weapon may be

⁸² For the purposes of this report, close contact refers to situations in which infected body fluids may come in contact with others. This includes health care professionals and family members who may provide care for those infected.

available for purchase.⁸³ In assessing the degree to which these agents have been studied in a munitions framework, agents are categorized in **Table 2** as weapon, research, or unknown. If an agent has been reported as successfully weaponized, it is listed as weapon. If an agent was a known target of a weapons program, but it is not reported as successfully weaponized, it is listed as research. If it is unknown whether an agent was the target of a weapons program, it is listed as unknown.

Examples. The bacterium *Yersinia pestis* causes the disease commonly known as plague. This bacterium is found naturally in many locations, with reservoirs in rodent populations. It causes publicized outbreaks in locations around the world (the United States averages 10 to 15 cases each year).⁸⁴ Thus, plague is considered easy to acquire by a terrorist and receives a + in this category in **Table 2**. There are several subcategories of plague, depending mostly upon the method of infection. Naturally occurring plague is usually transmitted by flea bites and has a mortality rate of 5% — 12% despite the availability of effective antibiotics.⁸⁵ Pneumonic plague is a more serious type of plague caused when the bacteria infect the lungs. Pneumonic plague is much more lethal than that caused by flea bites; the victims require isolation and intensive hospital care. Therefore plague receives a + for public health impact. There is a vaccine against plague, but it has not been shown to be effective against pneumonic plague. If an outbreak is detected, antibiotics can be taken prophylactically to prevent infection. Thus, plague receives a O for prophylaxis. Because pneumonic plague responds well to antibiotics only within the first 24 hours after symptom onset, it receives a O for resistance to medical treatment. In contrast to the type of plague transmitted by fleas, pneumonic plague is contagious through casual person-to-person contact. Therefore, each initially infected individual could eventually infect several others. This would allow a terrorist to bypass the technically challenging development of an aerosolizing device. Each infected person becomes a potential vector for the spread of the disease. Because of this, plague receives a + for ease of dissemination. Plague was reportedly studied by both the U.S. and former U.S.S.R. weapons programs.⁸⁶ The former

⁸³ Ken Alibek, a former high ranking official in the Soviet weapons program and a widely quoted expert on biological weapons, claims that many scientists who worked for the former Soviet Union's biological weapons program have been approached by groups interested in purchasing their expertise. See, for example, Ken Alibek, *Biohazard: The Chilling True Story of the Largest Covert Biological Weapons Program in the World — Told from Inside by the Man Who Ran It*, *op. cit.* pp. 271-272.

⁸⁴ Centers for Disease Control and Prevention, *Plague Fact Sheet*, available online at [<http://www.cdc.gov/ncidod/dvbid/plague/index.htm>].

⁸⁵ Thomas W. McGovern and Arthur M. Friedlander, "Plague," in *Medical Aspects of Chemical and Biological Warfare*, *op. cit.*

⁸⁶ The United States former biological weapons program reportedly did not weaponize plague, but only studied it as a research target. Stockholm International Peace Research Institute, *The Problem of Chemical and Biological Warfare, Volume I: The Rise of CB Weapons*, Stockholm: Almqvist & Wiksell, 1971.

U.S.S.R. reportedly successfully weaponized plague and is rumored to have developed antibiotic-resistant strains.⁸⁷

Anthrax is caused by the bacterium *Bacillus anthracis*. This bacterium occurs naturally in many locations around the world. Therefore in **Table 2**, anthrax receives a + for ease of acquisition. Untreated inhalational anthrax is nearly always fatal. The aggressive medical treatment victims received during the 2001 anthrax outbreak reduced the mortality rate to approximately 50% (five of eleven). Because of the high mortality rate and the need for hospitalization for treatment, inhalational anthrax rates a + for public health impact. Because the anthrax vaccine and antibiotics work prophylactically, anthrax receives a — in the prophylaxis category. Antibiotics are used against anthrax, but the success of this treatment depends on diagnosis shortly after onset of symptoms. Therefore anthrax receives a O for resistance to medical treatment in **Table 2**. Traditionally, it is considered difficult to produce the very fine particle size necessary to inflict mass casualties. However, to inflict casualties on a more modest scale (tens to hundreds), a cruder preparation with non-optimal particle size distribution may be sufficient. Therefore, for a small-scale attack, anthrax receives a + for ease of dissemination. Anthrax was reportedly successfully weaponized by both the U.S. and former U.S.S.R. programs. Antibiotic resistant strains could be developed. While this would increase the public health impact, the technical ability required to do this would decrease the ease of acquisition.

In 1984, the Rajneeshee cult successfully employed *Salmonella* Typhimurium in Oregon restaurants, sickening 751 people. This bacterium is ubiquitous, causing an estimated 40,000 cases of food poisoning in the United States each year. Therefore, salmonella receives a + for ease of acquisition in **Table 2**. Because salmonella usually does not require hospitalization, it receives a — for public health impact. There is no vaccine for salmonella. Because of the lack of a vaccine, salmonella receives a + for prophylaxis. Since antibiotic treatment for salmonella is well established, salmonella receives a — under resistance to medical treatment. Salmonella needs to be ingested, so the only effective route for dissemination would be through deliberate food, beverage, or water contamination. Therefore, *Salmonella* Typhimurium receives a — for ease of dissemination.

Toxin Agents Comparison

Toxins are poisonous substances that are produced by living organisms, including plants, animals, algae, and bacteria. These substances cause damage when introduced into the body. Often, toxin is the lethal agent in a bacterial infection, rather than the bacteria themselves. For example, intestinal infection with *Clostridium botulinum* is lethal due to the toxins that are exuded into the body, not simply because of the presence of bacteria. In some cases, these toxins can be produced in sufficient quantities and isolated from the organisms that produce them. Unlike living pathogens, toxins do not replicate. The human body is capable of developing antibodies to neutralize many toxins.

⁸⁷ Ken Alibek, *Biohazard: The Chilling True Story of the Largest Covert Biological Weapons Program in the World — Told from Inside by the Man Who Ran It*, op. cit.

Toxins are intermediate between biological and chemical agents in efficacy as weapons; requiring a greater amount of material than in the case of a biological agent, but less than required for a chemical agent. Toxins generally cause injury within hours of an attack. Therefore toxins may act more quickly than biological agents, which may take days or weeks to incubate, but more slowly than chemical agents, which generally act immediately. Toxins often have effects similar to chemical nerve agents, such as paralysis and nerve-related damage. Countermeasures for toxins resemble those for biological agents. Toxoid vaccines are used for prophylaxis and anti-toxins for patients after exposure.

Choice of Toxin Agents Assessed. The toxins chosen for inclusion in the matrix were compiled by comparing several sources including the BWC draft Compliance Protocol Annex A list,⁸⁸ the CDC Select Agent List,⁸⁹ the CDC Biological Diseases/Agents Listing,⁹⁰ the *NATO Handbook on the Medical Aspects of NBC Defensive Operations*,⁹¹ the U.S. DOD's *Medical Aspects of Chemical and Biological Warfare*,⁹² the Australia Group List of biological agents for export control,⁹³ the World Health Organization's *Preparedness for the Deliberate Use of Biological Agents*,⁹⁴ the U.S. DOJ's *An Introduction to Biological Agent Detection Equipment for Emergency First Responders*,⁹⁵ the former Soviet Union's bioweapons program, and the United States' former biological weapons program.⁹⁶ Toxins that appear on most lists were selected from the initial compilation, and then ranked. **Table 3** presents the toxins with the highest relative rank according to this analysis.

Criteria. **Table 3** categorizes toxin agents based on six criteria: ease of acquisition, public health impact, prophylaxis, resistance to medical treatment, ease of dissemination, and whether the toxin has been weaponized. Agents are listed in descending order of combined ranking with respect to the criteria. For further information on the methodology regarding criteria choice, ranking, and weighting,

⁸⁸ The rolling text for the draft BWC Protocol from February, 2001 was used. It can be found online at [<http://www.fas.org/bwc/papers/febannexI.htm#aann>].

⁸⁹ The Select Agent list is defined in 42 C.F.R. 73.4.

⁹⁰ The CDC Biological Diseases/Agents Listing can be found online at [<http://www.bt.cdc.gov/Agent/Agentlist.asp>].

⁹¹ *NATO Handbook on the Medical Aspects of NBC Defensive Operations AmedP-6(B)*, *op. cit.*

⁹² *Medical Aspects of Chemical and Biological Warfare*, *op. cit.*

⁹³ The Australia Group List of Biological Agents for Export Control can be found online at [http://www.australiagroup.net/en/control_list/bio_agents.htm].

⁹⁴ Found online at [http://whqlibdoc.who.int/hq/2002/WHO_CDS_CSR_EPH_2002.16.pdf].

⁹⁵ *An Introduction to Biological Agent Detection Equipment for Emergency First Responders*, *op. cit.*

⁹⁶ Toxins found in the former Soviet Union's and United States' former biological weapons program can be found in a summary developed by the Monterey Institute of International Studies from sources in the open literature. The summary is found online at [<http://cns.miis.edu/research/cbw/possess.htm>].

see **Appendix A**. See **Table 6** in **Appendix D** for technical data used to rate each agent.

Ease of Acquisition. Toxins must be extracted from the material in which the toxin was formed. Thus, acquiring toxins is more complicated than growing biological agents, but can be less complicated than synthesizing chemical agents. The production capacity needed to make enough agent for a terror event within a medium-sized, enclosed space could be developed in a basement lab, without access to a manufacturing plant.

A limiting factor is how ubiquitous the source of a toxin is. Some toxins are commercially available due to their dual-use nature;⁹⁷ the source plants or bacteria for other toxins are commercially available. In a few cases, neither the toxin nor its source is commercially available. To obtain these toxins one would need to find the plant, animal, bacteria or algae that produces the toxin in nature.

In the ease of acquisition column of **Table 3**, the symbol + denotes toxins for which the source of the compound can be found widely in nature, easily purchased or grown. The symbol O denotes toxins for which the source of the compound is purchased or grown with some difficulty. The symbol — denotes toxins for which the source of the compound cannot be purchased, is found only in few locations, or is grown with great difficulty.

Public Health Impact. Toxins can be incapacitating or lethal.⁹⁸ The variety of effects and methods of dispersal necessitate a more indirect estimation of the agent's impact. Again, the burden placed on the medical system will be used as the measurement for effect on the target. As an example, a toxin may have a low lethality but a high public health impact due to its effects.

In the public health impact column of **Table 3**, the symbol + denotes toxins that have a high, deleterious public health impact. The symbol O denotes toxins that have a more moderate, deleterious public health impact. The symbol — denotes toxins that have a relatively low, deleterious public health impact.

⁹⁷ Botulinum toxin is used commercially in dilute solutions as a medical treatment; several other toxins are commonly used in biomedical research.

⁹⁸ This distinction is made between different toxins, not between different types of C/B agents. For example, although *Staphylococcus aureus* enterotoxin B is generally considered to be an incapacitating agent, it is lethal at a concentration comparable to that necessary for the most lethal nerve gas, VX.

Table 3. Toxin agent comparison according to barriers to potential terrorist use

Toxins	Ease of Acquisition	Public Health Impact	Prophylaxis	Resistance to Medical Treatment	Ease of Dissemination	Weaponized
Abrin	+	+	+	+	O	Unknown
Shigatoxin	+	+	+	+	O	Unknown
Ricin	+	+	O	+	O	Weapon
<i>Clostridium perfringens</i> epsilon toxin	O	+	O	+	O	Weapon
<i>Staphylococcus aureus</i> enterotoxin B	O	+	O	+	O	Weapon
Trichothecene mycotoxins	—	O	+	+	+	Research
Aflatoxins	O	—	+	+	O	Weapon
<i>Clostridium botulinum</i> toxins	+	+	O	—	O	Weapon
Saxitoxin	—	+	+	O	O	Research
Tetrodotoxin	—	+	O	—	O	Unknown

Source: This table was prepared from compiled open source data. Congressional Research Service, 2002 (Updated 2004). See **Appendix D** for detailed data used to generate rating.

Note: See text for explanation of symbols. Breaks within the table group agents with roughly comparable rank.

Prophylaxis. Toxoid vaccines can be used to protect people against specific toxins. While many toxoid vaccines are available, few are licensed for general use, and supplies of these toxoid vaccines are generally small. Toxins against which the population is routinely vaccinated pose little threat and therefore have been removed from the analysis.⁹⁹

In the prophylaxis column of **Table 3**, the symbol + denotes toxins which have no prophylaxis. The symbol O denotes toxins with experimental prophylaxis lacking Food and Drug Administration approval. The symbol — denotes toxins which have licensed prophylaxis.

Resistance to Medical Treatment. Not all toxins have effective treatment. For some toxins, anti-toxin injections or other treatments are effective. Other toxins have no specific treatment available, but can be treated with supportive care such as mechanical ventilation or treatment for shock.

In the resistance to medical treatment column of **Table 3**, the symbol + denotes toxins that can only be treated using supportive care. The symbol O denotes toxins whose effects can be successfully ameliorated by a specific, established medical treatment. The symbol — denotes toxins that have documented anti-toxins available.

Ease of Dissemination. Toxins, like biological agents, can be weaponized in liquid or solid form, with the inherent difficulties of generating aerosols of appropriate particle size for efficient inhalation. Toxins can be delivered through contaminated food or drink or by aerosolization. Most toxin aerosols must enter the body through the lungs, eyes or broken skin to cause damage, although trichothecene mycotoxins can cause damage through intact skin. Toxins vary in their stability, which can complicate the ease with which they are disseminated.

In the ease of dissemination column of **Table 3**, the symbol + denotes toxins that can be delivered by skin contact. The symbol O denotes toxins that can be disseminated through both aerosolization and contamination of food or drink. The symbol — denotes toxins that only can be disseminated through either aerosolization or contamination of food or drink.

Weaponization. Some toxins were reportedly developed by either the Soviet Union's or the United States' former biological weapons program. While most of the toxin agents were only research targets, several toxins were successfully converted into military grade agents. Due to this research, the knowledge necessary to produce toxins efficiently and formulate them into warfare agents may be available for purchase. In assessing the degree to which these agents have been studied in a munitions framework, agents were categorized as weapon, research, or unknown. If an agent has been reported as successfully weaponized, it is listed as weapon. If an agent was a known target of a weapons program, but has not reported as successfully weaponized, it is listed as research. If it is unknown whether an agent was the target of a weapons program, it is listed as unknown.

⁹⁹ Tetanus toxin is an example of a toxin against which the population is routinely vaccinated. A terrorist attack using tetanus toxin would likely cause little harm.

Examples. Botulinum toxin is the most poisonous substance known.¹⁰⁰ It is produced by *Clostridium botulinum*, a ubiquitous soil bacterium. Therefore, in **Table 3**, it receives a + for ease of acquisition. Persons affected by botulinum toxin suffer nerve damage and paralysis, leading to asphyxiation and death. Although deaths rarely occur from naturally occurring botulism outbreaks, victims require intensive hospital care. Additionally even a small terrorist attack may overwhelm the capacity of local health facilities, resulting in many deaths. Therefore, it receives a + for public health impact. Because there is a toxoid vaccine for botulinum toxin, available in limited supply from the Centers for Disease Control and Prevention, it receives a O for prophylaxis. Botulism antitoxin can mitigate the effects of exposure, but there are limited available supplies. Supportive care including mechanical ventilation can also prevent death. Because of its well established medical treatment, it receives a — for resistance to medical treatment. Botulinum toxin is fairly stable, existing for extended periods at room temperature, but is inactivated by cooking. It can therefore be aerosolized or delivered via uncooked food or drink. It receives a O for ease of dissemination. Both the Soviet Union's and the United States' weapons program reportedly successfully weaponized this toxin.

Ricin is a very toxic compound found in castor beans. During the production of castor oil, bean mash with a 5 percent ricin content is produced. Recipes for extracting the ricin from this mash are available on the Internet. Because of the ready availability of both the raw material and the necessary information to refine the toxin, ricin receives a + for ease of acquisition in **Table 3**. Persons exposed to ricin exhibit different symptoms depending on the exposure route. Ingestion of ricin causes nausea, diarrhea, gastric hemorrhaging and shock, leading eventually to death. Injection of ricin produces severe internal necrosis and hemorrhage, which usually culminates in systemic collapse. Inhalation of ricin leads to irritation of airways and lungs, causing pulmonary edema and pneumonia. Because the progressive nature of the toxin's effects requires continual hospitalization and care, ricin receives a + for public health impact. An Investigational New Drug (IND) ricin toxoid could be made available. Consequently, ricin receives a O for prophylaxis. Exposure to large amounts of ricin is almost invariably lethal, as ricin acts rapidly and irreversibly, and lacks known treatment. Ricin receives a + for resistance to medical treatment. Ricin is very stable and can be stored in either purified or impure forms. Ricin can be used either as an aerosol or as a food or drink contaminant. It receives a O for ease of dissemination. The United States reportedly researched ricin under its former biological weapons program, and Iraq reportedly weaponized ricin.

Saxitoxin is a very toxic compound best known for its role in paralytic shellfish poisoning. It is produced by dinoflagellate marine algae. Because of the difficulties growing and collecting large amounts of toxin from the algae or from shellfish in which the toxin has concentrated, saxitoxin receives a — for ease of acquisition in **Table 3**. Persons who ingest saxitoxin suffer nerve damage and slow paralysis similar to botulinum toxin. Inhalation of saxitoxin causes a fast blockage of nerve impulses, leading to death within minutes. Saxitoxin receives a + for public health impact. There is no toxoid vaccine available for saxitoxin, and so it receives a + for

¹⁰⁰ The Working Group on Civilian Biodefense, "Botulinum Toxin as a Biological Weapon," *Journal of the American Medical Association*, Vol. 285, Feb. 28, 2001, pp. 1059-1070.

prophylaxis. It is difficult to successfully treat victims within the necessary time window dictated by inhalation of aerosolized saxitoxin. Supportive care including mechanical ventilation can prevent death. Because of this established treatment, saxitoxin receives a **O** for resistance to medical treatment. It can be used to contaminate food or drink or as an aerosol. This flexibility gives saxitoxin a **O** for ease of dissemination. The U.S. Central Intelligence Agency researched the use of saxitoxin as a covert weapon, but it is unlikely to have been developed as a weapon for military use.¹⁰¹

Discussion

Potential Uses of Framework

Many expert analyses focus on the use of C/B agents to cause mass casualties through catastrophic terrorism. In this view, C/B agents that can be mass produced, are contagious, or are markedly stable are identified as the greatest threats. Therefore, government policy towards C/B terrorism has been designed to reduce the impact of C/B agents, such as nerve agents, smallpox, and anthrax, that possess these specific qualities. While some of these agents have been used in terror attacks, this analysis of the potential for small-scale use leads to a different assessment of C/B agent threat. C/B agents that were considered high threats in other frameworks appear to present a lesser threat when viewed in the small scale attack context. Conversely, C/B agents that were considered of lesser threat when considering mass casualty attacks may be ranked more highly in the small scale context, as barriers to mass use may be missing when the agent is used on a small scale. Because of these differences, policies designed to protect against catastrophic C/B attack may not provide equivalent protection against small scale C/B attack.

A potential use for the above framework is to help prioritize approaches to address the threat presented by small scale use of C/B agents. This analysis provides information relevant to the formation of general approaches to reduce the threat from terrorist use of different C/B agents, as well as information that may allow policymakers to reduce the dangers from specific agents. For example, policymakers may wish to develop specific remedies, via research targeted towards developing cures, prophylaxis, and detection equipment, or more efficient public health mechanisms for detecting and treating the agents towards the tops of these matrices. Because the agents analyzed in this framework are those which appear in a preponderance of past assessments, they represent a subset of potential C/B agents. Other dangerous agents which may be amenable to similar analysis have not been included. For example, newly emerging diseases, such as Nipah virus and SARS, may pose a future threat, but have not been included in past assessments. Therefore while policymakers may find this framework useful in formulating policy, more detailed analysis may be required when refining policy alternatives.

¹⁰¹ U.S. Senate. *Unauthorized Storage of Toxic Agents: Hearings before U.S. Senate Intelligence Committee*, 94th Cong, 1st Sess., Washington, DC: U.S. Senate, September 16-18, 1975.

Another potential use of this framework is to qualitatively highlight the effects that different policies may have in reducing C/B vulnerability. This overview indicates which agents of concern might be amenable to particular countermeasures. For example, policymakers may wish to focus on prophylaxis of toxins to reduce the threat that their use by terrorists would present. By reviewing the data presented in this assessment framework, policymakers might identify toxins for which no approved vaccine exists. This might aid in prioritizing regulatory review or directing research funds to develop new toxoid vaccines. Similarly, by weighing and considering the ease of acquisition of C/B agents, for example, it may become apparent which agents are susceptible to regulatory control, perhaps because of their development for industrial use, and which agents might not be, perhaps because of their endemic nature. This may aid in developing additional policy against C/B terrorism.

Another application for this framework might be to develop threat-reduction approaches for specific agents. Depending on the agent, funding for research and development, regulation, or directed advances in public health may lower the threat posed. For example, regulation regarding the sale of the source of the toxin abrin might be considered an effective approach to reducing its ease of access, thereby lowering the threat posed by this toxin.

The data presented in this framework, and in the appendices, may also serve as a resource to develop other more specialized frameworks. Policymakers might reorder agents based on specific criteria, for example, response to medical treatment, based on the data provided in this report. Some may wish to emphasize certain criteria over others, providing a nonequivalent weighting to the different criteria. These manipulations might provide legislators with more tailored matrices for use in exploring policy options.

For example, while the agents in this assessment have been sorted by considering the difficulties a terrorist group might encounter in developing an agent, sorting according to specific priorities might present a different final product. Especially in the cases where specific knowledge is held about criteria presented here, sorting the agents while excluding certain criteria would provide other insights. For example, Marburg hemorrhagic fever is ranked lower on **Table 2** because of the difficulty in obtaining the causative virus. In the current sorting algorithm, this significant disadvantage to its use determines its ranking below other agents which lack any comparable disadvantage. If, for reasons outside the confines of this assessment, it was known that Marburg virus was available to a terrorist organization, resorting this matrix without regard to the ease of acquisition would place Marburg hemorrhagic fever at the top of this matrix. Thus, the risk posed by Marburg hemorrhagic fever would be increased under those conditions.

Whether an agent has been weaponized, or was the target of a weapons program, was not used as a primary ranking factor. Rather it was used to adjust the relative ranking of agents that are comparably rated. Thus, two agents that have the same relative numbers of —, +, and O in the matrix would be equally rated. If one of these agents was known to be successfully weaponized, while the other was never studied, then the agent known to be weaponized would be ranked higher on the matrix. The exclusion of weaponization status as an independent category might be

seen as inappropriate if there are credible reports of information or technology transfer from a bioweapons program to a terrorist group. In such an event, it might be more appropriate to directly include the weaponization status into the ranking and sorting procedure.

Deviations From Assumptions

Several assumptions, mainly about the resources and skills of the groups attempting to develop C/B agents, have been made in developing this framework. If these assumptions are invalid, then the results of this report will be less applicable. For example, if a terrorist group is unable to recruit or train members to the degree necessary to reproducibly and repeatedly synthesize or grow C/B agents, then the effort expended in acquiring sufficient amounts of the C/B agent may be much higher than estimated through this framework. If a terrorist group lacks financial means, a similar increase in the difficulty of manufacture might occur. This could cause the criteria to have distinctly unequal weights, where the ease of acquisition would dominate all other criteria.

If a terrorist group is sponsored by a nation-state, then the capabilities of the terrorist group may be much greater than those assumed here. For instance, ease of acquisition and ease of dissemination could be drastically different, as technology transfer from the sponsor to the terrorist group could remove these barriers and thus remove the influence of these criteria from the ranking. A terrorist group planning a mass, city-wide assault using a C/B agent might face difficulties in the scale of material and logistics necessary, and the threat might more closely parallel previous assessments of mass-dissemination.¹⁰²

One policy issue regarding C/B defense is that threat assessments rely on probability estimates. This means that while analysts may speak of a likelihood of an agent being used, no one, besides terrorists who use them, can speak with authority about the agents that will be used. Terrorists may act opportunistically; if presented with an agent, either purchased or stolen, they may use that agent even if it is not optimal for their purposes. Purchase or theft of a C/B agent alters relative threat assessments, as many of the factors contributing to the relative threat are weighted differently. Consequently, while a relative threat assessment is a useful framework for rational discussion, it cannot be used as a definitive statement on the likelihood of future C/B use.

Terrorist Motivation-Specific Factors

The above analysis assumes a terrorist group has decided to use a chemical, biological, or toxin weapon and is considering the relative potential of all of these agents equally. However, this analysis does not necessarily reflect all factors that may contribute to the choice of a particular agent. The following section explores

¹⁰² See U.S. Congress, Office of Technology Assessment, *Technologies Underlying Weapons of Mass Destruction*, *op. cit.*

other factors that a specific terrorist group might consider, based on its objectives or motivations.¹⁰³

Potential for Covert Deployment

Some experts claim that it is increasingly likely that a terrorist group would not claim responsibility for a C/B attack.¹⁰⁴ The incidence of catastrophic, anonymous terrorist attacks is projected to increase, as terrorist groups organize around issues that have less local, concrete political goals, but instead are more ideologically driven.¹⁰⁵ This tendency complicates analysis of the bioterror threat, as terrorists may successfully covertly attack using a disease found within the United States. With a small outbreak, a lack of any claim of responsibility could raise the question of whether the outbreak was a terrorist act or a simply an unusual natural epidemic. For example, releasing Ebola virus in a building in New York City would immediately be treated as a terrorist attack, regardless of whether any group claimed responsibility. On the other hand, the salmonella attacks perpetrated by the Rajneeshees were not identified as a deliberate release until over a year after the event when a member of the cult confessed to the crime. One of the factors that led the cult leaders to choose salmonella was that it was a less traceable agent, in the hopes that their act would remain undiscovered.¹⁰⁶ Since the probability that a terrorist group will opt for covert, rather than open, deployment may not be known, it is difficult to factor this choice into an analysis.

A terrorist group could choose to deploy a biological agent covertly because of the advantages the group would gain. An agent release disguised as a natural outbreak could allow for trial runs to be conducted before a large attack as was done by the Rajneeshees. Such trials could test the government response to an apparently natural outbreak, possibly allowing terrorists to further refine attack plans to exploit weaknesses uncovered during the trials. By using a local pathogen, there may be serious, though reasonable, disagreement between public health and law enforcement officials with respect to the outbreak's origin, leading to over- or under-reaction to the outbreak. Finally, during a small-scale outbreak, questions over the magnitude of local, state, or federal response may arise, to the potential advantage of a terrorist wishing to instill confusion at low cost.¹⁰⁷

¹⁰³ For more on this topic, see CRS Report RL31831 *Terrorist Motivations for Chemical and Biological Weapons Use: Placing the Threat in Context* by Audrey Kurth Cronin.

¹⁰⁴ National Commission on Terrorism, *Countering the Changing Threat of International Terrorism*, August 2, 2000, Chapter 3.

¹⁰⁵ National Intelligence Council, *Global Trends 2015: A Dialogue About the Future with Nongovernment Experts*, December 2002.

¹⁰⁶ Another factor involved in the Rajneeshee attack was their reported wish to influence local elections by incapacitating, rather than killing, the electorate. W. Seth Carus, "The Rajneeshees (1984)" in *Toxic Terror: Assessing Terrorist Use of Chemical and Biological Weapons*, *op. cit.*

¹⁰⁷ Coordination between federal agencies and the preparedness of state and local responders have been highlighted in testimony by the GAO. Testimony of Janet Heinrich, Director, (continued...)

The Department of Homeland Security has developed and deployed a system of biological weapon detectors called BioWatch.¹⁰⁸ The BioWatch program has installed detectors in more than thirty cities. They are primarily designed to detect the catastrophic release of biological weapons, not the release of small amounts of biological weapons. In October 2003, the BioWatch system in Houston, TX detected aerosols of *Francisella tularensis*. Subsequent analysis revealed that this signal arose from detection of naturally occurring bacteria.¹⁰⁹ Considering the apparent sensitivity of this detection system, it is possible that small-scale releases might be detected. Determining whether such a signal was from naturally occurring bacteria, or from a small-scale act of terrorism, may be challenging. Since the federal response to an act of terrorism will likely be substantially different than to detection of naturally occurring bacteria, quickly differentiating between the two events is important.

Range of Lethality and Impact

The media attention given to civilian deaths may induce a terrorist to prefer an agent with high fatalities over agents that inflict a high number of casualties, but low fatalities, if they believed that this would garner more media attention. Terrorists may believe that such media coverage of terror events may further recognition of their cause or increase the impact of their actions.

A potential C/B agent user is also faced with the possibility that the C/B agent may kill the user either during an accident in the preparation stage or during dissemination. The events of September 11, 2001 have shown that there are individuals motivated enough to die for their beliefs who wish to strike at assets within the United States.¹¹⁰ Consequently, the idea that a C/B agent might be too lethal or too toxic to be used, a belief held in some previous treatments of this subject, should be reexamined. If one assumes that the user of the C/B agent is willing to die during its use, casualties and fatalities from an agent's dissemination can be maximized, because an agent lacking both treatment and prophylaxis can be used.

Similarly, an organization with a supply of members willing to be placed at risk during the manufacture of a biological agent can produce large amounts of an

¹⁰⁷ (...continued)

Health Care — Public Health Issues, before the House Committee on Government Reform, October 5, 2001. U.S. Congress, General Accounting Office, *Bioterrorism: Coordination and Preparedness*, GAO-02-129T, October 5, 2001.

¹⁰⁸ For more information about the BioWatch program, see CRS Report RL32152 *The BioWatch Program: Detection of Bioterrorism* by Dana A. Shea and Sarah A. Lister.

¹⁰⁹ Robert Roos, "Signs of Tularemia Agent Detected in Houston Air," *CIDRAP News*, October 10, 2003.

¹¹⁰ Not all terrorists who might be willing to die committing an act of terrorism would be likely to commit an act of chemical or biological terrorism. Cultural and religious norms regarding chemical or biological weapons' use, as well as the potential for significant suffering from self-infection or exposure, may limit the number of individuals willing to engage in chemical or biological terrorism.

incurable pathogen by training members in the specific techniques necessary to grow that agent. The threat of self-infection combined with the need for advanced technical knowledge is often cited as another barrier to terrorist development of biological agents. The use of trained technicians willing to die would allow production of agents under improvised safety conditions. By training others to act as technicians, a terrorist organization could reduce the danger to its knowledgeable scientists, distribute the techniques for developing a pathogen program among the members of the organization, and increase the rate of pathogen production.

It is not necessary for members of a terrorist group to be without regard for their lives to develop C/B agents. Terrorist groups with access to prophylaxis, especially prophylaxis with limited distribution, could develop biological agents at less personal risk. Alternately, effective mechanical protection might guard terrorists manufacturing chemical agents. Even if the civilian population has some access to the vaccine or other prophylaxis, the impact of dissemination would still be very high if these materials are uncommon. Some biological and toxin agents have vaccines available to select individuals, such as troops or research scientists, but not the general public.

Therefore, some terrorists may find highly lethal, incurable agents to be most effective in achieving their objectives. However, as seen in the salmonella attack, not all terrorists choose the most lethal agent available. The cult leaders chose salmonella because a nonlethal agent was deemed sufficient to achieve the desired outcome of decreasing voter turnout in a local election.¹¹¹

Contagious Dissemination

Pathogens contagious through casual contact may be preferred by some terrorists. One scenario could involve dissemination of a contagious pathogen through self-infection. Self-infection is especially important to consider because it is a low-technology method for highly selective targeting of initial infection points. A terrorist who is contagious could choose to fly through multiple airports in a single day, potentially causing many different foci of infection to erupt. While the terrorist would have to endure the full effects of the untreated illness, the consequences of such a method of distribution could be high. Some experts claim that the progression of the illness would prevent the terrorist from being well enough to proceed with such a plan. Other experts have cited historical natural outbreaks on public transportation, such as trains, as evidence that individuals with diseases in the contagious stage have been able to travel and infect others.¹¹²

The lack of controllability of contagious pathogens in comparison to other biological agents may serve as a deterrent to groups unwilling to engage in indiscriminate infection. For example, terrorist groups that have a constituency in or near the exposure area might not be willing to risk infection of their constituents.

¹¹¹ This case study shows the importance of developing further refined risk assessment based on the known goals, motivations, and capabilities of specific terrorist organizations.

¹¹² Dr. William Bicknell at "Bioterrorism and Smallpox: Ring Containment, Mass Vaccination, or Individual Choice?" Cato Institute, June 4, 2002.

Alternately, apocalyptic groups or terrorist groups acting geographically distant from their support may not view the lack of controllability as a significant drawback.

Previous Use of C/B Agents

Some terrorists, lacking knowledge of potential agents, may choose C/B agents because they have been used in the past. Terrorists may look to previous attacks to learn which C/B agents were effective and how the C/B agents were dispersed. The difficulties in performing a successful C/B attack are illustrated through the examples of the Rajneeshees' 1984 salmonella attack and Aum Shinrikyo's 1995 sarin attack. Both groups attempted to develop several different C/B agents before being successful.¹¹³ A terrorist could view past examples as decreasing the need to extensively test their C/B agent, since successful use had already been previously demonstrated.

Significant media attention may influence C/B agent choice. In the case where the media has reported widely on a C/B agent, more information is available regarding the strengths and weaknesses of an agent's use. While the C/B agent may not be optimal for the terrorist group's purpose, easily available information may provide a lower barrier than that provided by the group investing its resources in independent research for a more optimal C/B agent. Thus, there may be bias towards choosing those C/B agents which receive publicity.

Some C/B agents have garnered a reputation among extremist groups. Such a reputation, regardless of its basis in fact, may influence choice of agents. For example, ricin has been promoted by domestic paramilitary groups as a "silent tool of Justice."¹¹⁴ One of the factors that led members of the Minnesota Patriots Council to choose ricin over other alternatives was apparently such promotion.¹¹⁵

Source of C/B Agents

Among the most important variables to a terrorist choosing an agent is what agents are available to the group. Regardless of the ideal preference of a terrorist group, if the C/B agents available to it are limited, the group will choose from among those available.

From a Manufacturing Site. Some chemical agents are used commercially in manufacturing, water treatment and other industries. Theft of such agents in bulk from such a facility is of special concern to law enforcement officials. Due to the large volumes of agents used in many industrial processes, the regular rail and truck shipments of chemicals are also potential sources for terrorists. Before September 11, 2001, the chemical industry had been heavily criticized for its low plant security. The American Chemistry Council, a chemical trade organization dedicated to best

¹¹³ *Toxic Terror: Assessing Terrorist Use of Chemical and Biological Weapons, op. cit.*

¹¹⁴ Jonathan B. Tucker and Jason Pate, "The Minnesota Patriots Council" in *Toxic Terror: Assessing Terrorist Use of Chemical and Biological Weapons, op. cit.*

¹¹⁵ *Ibid.*

practices, has increased its member security requirements in response to recent events. For further information on chemical plant security, see CRS Report RL31530, *Chemical Plant Security*, by Linda-Jo Schierow.

From a Natural Source. The ease with which naturally occurring pathogens and toxins can be recovered from nature is a topic of much debate. Their natural prevalence is one of the most important criteria in determining the relative threat. There are strong differences in opinion regarding how easy it is to isolate microbial pathogens from nature. Because many biological agents are widely found in nature, covertly collecting these agents is not viewed as difficult. However, some experts claim that it is difficult to isolate pathogens with high virulence from these environmental samples.

Disease epidemics, either among humans or animals, may also be sources for pathogens. Some experts assert that obtaining pathogens from a disease outbreak would be difficult. They point to the efforts public health officials exert to identify the source of the disease during an outbreak.¹¹⁶ Other experts contend that the availability of pathogens during an outbreak is high, as any victim of the epidemic is a plentiful source of pathogens, not just the initial case. Further complicating debate on the topic is the prevalence of viral outbreaks in countries with limited health care systems. In 2002, an outbreak of Crimean-Congo hemorrhagic fever on the Afghanistan-Iran border occurred over a three-month period with multiple outbreaks among humans and animals.¹¹⁷ Epidemics such as this could be an ample source of pathogenic material, provided that the terrorist group was international in scope or had support among hospital staff in the outbreak region. Terrorist groups which infiltrate into hospital infrastructure, laboratory production, and other medical positions is an area of great concern. Laboratory workers handle many tissue and blood samples containing potential pathogens. These samples could be used as a starting point for growing biological agents.

From a Culture Collection. Culture collections are repositories of bacteria and viruses maintained typically for scientific research.¹¹⁸ In the past, culture collections have been largely unregulated. For example in 1995, Larry Wayne Harris was able to fraudulently purchase plague bacteria from a private germ bank, the American Type Culture Collection. This event caused great concern among health and law enforcement officials, and resulted in greater oversight and regulation of the

¹¹⁶ Public comments of Jonathan B. Tucker at "The Case for a Biosecurity Treaty" briefing for congressional staff, June 3, 2002. See also, Jonathan B. Tucker, "Preventing Terrorist Access to Dangerous Pathogens: The Need for International Biosecurity Standards," *Disarmament Diplomacy*, No. 66, September 2002.

¹¹⁷ See "Virus of Deadly Disease Spreads in Iran," *The Associated Press*, May 23, 2002 and Ted Anthony, "Outbreak of Hemorrhagic Fever Reported at Afghan-Iran Border," *The Associated Press*, June 6, 2002.

¹¹⁸ There are also toxin collections. Toxins do not reproduce, and so the purchase of small amounts of toxins from a collection is not as potentially dangerous as the purchase of small amounts of microbial pathogens. On the other hand, the availability of toxin-producing agents, such as aflatoxin-producing mold strains, through such a collection would raise concerns similar to those surrounding culture collections.

transfer of pathogens.¹¹⁹ This higher level of oversight has not been duplicated worldwide. The World Federation of Culture Collections, an international organization that indexes culture collections, has established member guidelines to adopt best practices and follow domestic and international regulation with respect to pathogens.¹²⁰ However, approximately two-thirds of the world culture collections are not members of this federation.¹²¹ Additionally, many culture collections are not financially secure. This situation may provide the opportunity for a wealthy terrorist group to acquire seed microbes from a culture collection which has well-characterized pathogens.

Manufacture and Preparation of C/B Agents

Most experts agree that terrorist groups lacking specialized training and knowledge in the weaponization of C/B agents will likely produce sub-optimal quality agents. These C/B agents may be more likely to degrade during storage than C/B weapons produced by nation-states. This degradation may lead terrorist groups to produce the agent immediately before the attack or to plan smaller scale attacks, so as to minimize agent loss.

The preparation of C/B agents for dissemination will also play a significant role in the effectiveness of a terror attack. Terrorist groups lacking experience and specialized knowledge will likely be unable to generate weaponized C/B agents, and instead will be forced to utilize cruder, less refined mixtures of C/B agent and other material, such as non-viable pathogens and media or residual solvent. Dissemination of C/B agents using adapted technologies, such as improvised aerosolization devices, is unlikely to produce optimal particle size distributions, thereby limiting their effect. Therefore, the effectiveness of a C/B attack by terrorists is likely to be significantly lower than that predicted under optimal conditions. These factors may lead to the appearance of a smaller scale attack, even if a catastrophic, mass casualty attack is attempted.

The above considerations may significantly influence the C/B agent choice of a terrorist group. C/B agents which lack well documented storage procedures or manufacturing information may be avoided by a terrorist group even if the C/B agent would otherwise be more highly ranked. Similarly, reduced dissemination effectiveness may dissuade terrorist groups from selecting C/B agents difficult to manufacture or store, due to concerns about producing and stockpiling enough C/B agent.

¹¹⁹ The Antiterrorism and Effective Death Penalty Act of 1996 (P. L. 104-132) requires the Secretary of Health and Human Services to create the Select Agent list and regulate these agents' transfer within the United States. This part of this act closed the loophole allowing Harris's purchase of a Select Agent pathogen.

¹²⁰ For more information about the World Federation of Culture Collections see their website at [<http://www.wfcc.info>].

¹²¹ Michael Barletta, Amy Sands and Jonathan B. Tucker, "Keeping Track of Anthrax: The Case for a Biosecurity Convention," *Bulletin of the Atomic Scientists*, May/June 2002.

Policy Issues

Current Regulation

International Regulation. The development, proliferation, and use of chemical and biological weaponry are closely regulated. The United States is a signatory to both the Biological Weapons Convention (BWC) and the Chemical Weapons Convention (CWC), and is actively involved in their implementation.¹²² Both the BWC and CWC prohibit offensive C/B development, as well as provide proliferation barriers to states not possessing a C/B capability. CWC international implementation is overseen by the Organization for the Prohibition of Chemical Weapons.¹²³ Additionally, the United States and 32 other nations participate in the Australia Group, an organization developed to voluntarily harmonize national export controls on chemical weapon precursor compounds, dual-use equipment, and biological agents that could be used to develop chemical and/or biological weapons capability.¹²⁴

Domestic Regulation. The use or threatened use of a weapon of mass destruction is illegal. More specific restrictions apply to chemical and biological weapons.¹²⁵ It is unlawful to knowingly develop, produce, possess, use, or threaten to use a chemical weapon. However, various governmental agencies and departments are exempted, as are research and possession for peaceful purposes.

In the U.S., it is a criminal offense to use or threaten to use, develop, produce, stockpile, acquire, or retain biological weapons, or transfer biological agents without registration. Exceptions are made for *bona fide* research, prophylactic, medical, and diagnostic activities. Also, the Department of Health and Human Services is required to create and maintain a list of those agents (the Select Agent list) dangerous to the public health.¹²⁶

The Public Health Security and Bioterrorism Preparedness and Response Act of 2002 (P.L. 107-188) requires the Secretary of Health and Human Services to create a registry of all persons possessing agents on the Select Agent list and a registry containing identifying characteristics of the agents possessed. It also requires the

¹²² For an overview of the United States' implementation of the CWC and BWC provisions, see CRS Report RL30033, *Arms Control and Nonproliferation Activities: A Catalog of Recent Events*, coordinated by Amy F. Woolf.

¹²³ More information on the Organization for the Prohibition of Chemical Weapons can be found at [<http://www.opcw.org>].

¹²⁴ More information on the Australia Group can be found at [http://www.australiagroup.net/index_en.htm].

¹²⁵ For an overview of the laws surrounding chemical and biological agents see CRS Report RL32220 *Biological and Chemical Weapons: Criminal Sanctions and Federal Regulations* by Michael J. Garcia, CRS Report RL32158 *Chemical Weapons Convention: Issues for Congress*, by Steven R. Bowman, and CRS Report RL31059 *Biological Weapons: A Primer* by Steven R. Bowman.

¹²⁶ The Select Agent list is defined in 42 C.F.R. 73.4.

Secretary of Agriculture to create a similar registry regarding agents deemed to be an agricultural hazard. For more on P. L. 107-188, and specifically on the new Select Agent requirements in that law, see CRS Report RL31263, *Bioterrorism: Legislation to Improve Public Health Preparedness and Response Capacity*, by C. Stephen Redhead, Donna U. Vogt and Mary E. Tiemann.

Dual-Use Concerns

Dual-use technologies are technologies that have legitimate uses, but are adaptable for terrorist purposes and can provide terrorist groups with ready-made, proven technology to aid in their C/B agent production. An issue of great concern to anti-proliferation agencies is the potential of dual-use technology to jump-start access to C/B production. The export and import of dual-use technologies is primarily addressed through trade regulation. The U.S. Department of Defense, the U.S. Department of State, and the U.S. Department of Commerce are all involved in determining, regulating, and implementing export controls for dual-use technology. Additionally, the United States supports and participates in the Australia Group's anti-proliferation campaign. These policies are directed primarily at nation-level programs and only partially block an individual's access to dual-use technology, especially when the purchases do not cross national borders.¹²⁷

Addressing the issue of dual-use technology is complicated for analysts, regulators, and policymakers. Strict control of C/B dual-use technology could provide an accurate accounting of such sales, but this level of control may greatly impact both the business and health sectors. Pharmaceutical and chemical industries would likely fall under any regulations dealing with chemical threats, while hospitals, medical laboratories and biotechnology firms would likely become further regulated. Academic research into a number of fields, including molecular biology, chemistry, microbiology, virology, neuroscience and others, might be significantly affected as well.¹²⁸ The addition of such technology regulation might be successful at lowering the risk of C/B terror, but could come at a high regulatory burden and economic cost.¹²⁹

¹²⁷ Under Project BACUS, the Defense Threat Reduction Agency successfully built a C/B agent production facility in Nevada from dual-use technology without drawing regulatory attention. As reported in Judith Miller, Stephan Engelberg, and William Broad, *Germs: Biological Weapons and America's Secret War*, New York: Simon and Schuster, 2001, 121.

¹²⁸ After the anthrax letters were typed as an Ames strain, the veterinary school at Iowa State University decided to destroy its collection of anthrax strains, which had been collected since 1928. See Katie Norris, "Iowa State U. Officials Don't Regret Destroying Their Anthrax Sample," *Iowa State Daily*, November 27, 2001. Other researchers in the field also have encountered more complicating factors in their work as CDC oversight and FBI inquiry are now more pronounced. See Melinda Deslatte, "Anthrax Researcher Finds More Complications in Work Since October," *Associated Press*, January 31, 2002.

¹²⁹ See CRS Report RS21422 *Dual-Use Biological Equipment: Difficulties in Domestic Regulation* by Dana A. Shea.

New Multinational Regulation Options

Some experts advocate, as a means of controlling C/B terror, a biosecurity treaty to further enhance the transparency of national biodefense and industrial biotechnology programs.¹³⁰ One aspect of this proposed, evolving framework is a harmonization of internal national standards to regulate the handling, storage and transfer of biological pathogens. Signatories would determine a list of covered pathogens and set general guidelines. Each signatory would then develop specific methods to implement the guidelines. In theory, this would lower the probability that a terrorist could acquire a dangerous pathogen from a foreign germ bank for use in the United States. Proponents of such a treaty point to the largely successful use of regulatory inspections and control of raw starting materials in stemming transfer of radiological and nuclear materials from nation states to terrorist groups. They also cite the short travel time between distant points as a factor which requires international cooperation and attention to combat potential bioterrorism.¹³¹

It is not clear whether regulation on the nation-state level could provide significant barriers to small-scale production. Nation-state-level mechanisms have been relatively successful at stemming nuclear proliferation because of the technical difficulties involved in developing an infrastructure capable of manufacturing a nuclear bomb, combined with the need for localized, easily detected and tracked nuclear material. However, revelations regarding the dissemination of nuclear weapon technology from Pakistan highlight some of the difficulties in this approach even with nuclear weapons. Proliferation of chemical and biological agents is not as limited by required technology as nuclear weapons, and source material is much more readily available. Also, because of the dual-use nature of the technologies used with C/B agents, export control of chemical and biological weapons development is difficult. For example, Iraq was able to significantly expand its chemical and biological weapon capabilities before the first Gulf War through the purchase of dual-use technology. Opponents of further regulation by treaty emphasize the ease in obscuring the purpose of dual-use technology and the difficulty in conclusively identifying a C/B program. Additionally, there are serious concerns with international regulatory inspections, including the transparency of on-site inspections, the degree to which inspectors should be allowed to document and access commercial sites, because of concerns over protecting proprietary information, and the practicality of a challenge inspection system.¹³²

There is also concern that multinational regulation would not adequately address the C/B terrorist threat. Some analysts point out that export and import controls prevent only the transfer of such items or technology over international borders, and

¹³⁰ See Michael Barletta, Amy Sands and Jonathan B. Tucker, "Keeping Track of Anthrax: The Case for a Biosecurity Convention," *op. cit.* and Jonathan B. Tucker, "Preventing Terrorist Access to Dangerous Pathogens: The Need for International Biosecurity Standards," *op. cit.*

¹³¹ Christopher Chyba, "Toward Biological Security," *Foreign Affairs*, May/June 2002.

¹³² For an overview of the issues surrounding international inspections, see CRS Report RL31559, *Proliferation Control Regimes: Background and Status* by Sharon A. Squassoni, Steven R. Bowman, and Carl E. Behrens.

do little to address C/B agent development within the country. They contend that domestic terrorist groups, or international groups which establish themselves within the United States, would be unaffected by enhanced multinational cooperation and transparency.

Prevention Versus Consequence Management

Law Enforcement Options. The approach that U.S. law enforcement agencies take towards counterterrorism is still evolving. FBI Director Mueller has stated that the FBI is shifting its counterterrorism efforts from a reactive philosophy to a proactive one.¹³³ As examples of this shift, Director Mueller pointed to efforts to restrict fund-raising efforts of terrorist groups and increased counterterrorism intelligence gathering. This approach is based on preventing future terrorist attacks, but it is unlikely that all possible attacks can be discovered, prevented, or planned for. Secretary of Defense Rumsfeld is reported to have stated, "It is physically impossible to defend at every time, in every place, against every conceivable technique." Vice President Cheney and FBI Director Mueller have reportedly stated that another terrorist attack is inevitable.¹³⁴

A related approach is deterrence. This approach has generally worked well at a nation-state level. For example, during the first Gulf War, coalition forces faced an adversary who apparently chose not to use the chemical, biological, and toxin weapons in its possession. It has been argued that Iraq was deterred from using these weapons by a veiled threat of massive retaliation.¹³⁵ It is less clear that deterrence would be effective against a terrorist group. In particular, international agreements and threats of massive retaliation are unlikely to deter a terrorist group that is willing to deploy a C/B agent anonymously and has no identifiable infrastructure vulnerable to counterattack.

Some policymakers may suggest increasing the resources devoted to investigating the incidents and prosecuting the perpetrators. This approach of deterrence on an individual scale is common in law enforcement. In the case of bank robberies, for example, it is widely believed that identifying, arresting, and punishing bank robbers is effective at deterring others who might be contemplating a similar crime. Criminal prosecution derives its deterrence value from the wish of the assailant to succeed at the event and escape. This approach may be adequate against some terrorist groups; however, it is unlikely to deter groups with members willing to die during action or groups that insulate the leaders and planners from those carrying out the attack. Hence, normal forms of policing may be inadequate to deal with those terrorists who choose suicide or place low value on escape. Proactive measures, such as intelligence gathering or infiltration of terrorist groups, may be the more effective approach to prevent suicide attacks.

¹³³ Robert Mueller, Testimony before the Senate Judiciary Committee, June 6, 2002.

¹³⁴ David Westphal, "Rumsfeld: Terrorists' Access to Deadlier Weapons Inevitable," Scripps Howard News Service, May 21, 2002.

¹³⁵ Judith Miller, Stephan Engelberg, and William Broad, *Germs: Biological Weapons and America's Secret War*, *op. cit.*

Health Care Options. Policymakers may want to address whether to focus on prophylaxis against specific diseases or to address the bioterror threat through a broader approach. The targeted approach is illustrated by Secretary of Health and Human Services Thompson, who is reported as saying that the government's position with respect to smallpox vaccine is that "every man, woman and child will have a vaccine they can say has their name on it."¹³⁶ Vaccines for many diseases are available under Investigational New Drug protocols, and there has been legislative interest in spurring private sector research into the development of new vaccines and treatments.¹³⁷ With development and large-scale availability of vaccines for bioterror agents, the threat posed by those specific agents is diminished.

Proponents of a targeted approach claim that additional vaccines will appreciably lower the global threat as fewer pathogens become viable mass-casualty agents. Critics argue that the vulnerability to agents lacking a vaccine would be fundamentally unchanged under the targeted approach. Furthermore, the decision of what agents to protect against may reflect the ease of vaccine production or other factors rather than the risk an agent will be used. It is not certain that a vaccine can be produced in a timely manner for the highest threat agents. A further criticism of the specific vaccine approach is the logistical effort required to vaccinate the population. The cost of repeatedly vaccinating large populations may offset the economic benefit of providing specific prophylaxis for many agents. Finally, as seen in the smallpox vaccination efforts, the perceived risk from vaccination must be weighed against the potential risk of biological attack.

A broader approach is advocated by other experts, who claim that the best defense against a bioterror attack is to increase the capacity of the public health sector to treat ill people, track emerging diseases, and provide care to those made ill during a bioterror attack. Proponents of an increase in public health advocate that this approach provides an equal and general application to most naturally occurring diseases and accidents.¹³⁸ Yet critics contend that increasing the nationwide quality of public health care would be too expensive to implement at the required level and to sustain indefinitely. Furthermore, the threat posed by untreatable agents would remain unchanged, as this approach would not attempt to discover new specific treatments.

¹³⁶ Susan Okie and Justin Gillis, "U.S. Mounts Smallpox Vaccine Push; Officials Want a Dose for Every Person in the Country by the End of 2002," *The Washington Post*, October 28, 2001.

¹³⁷ For example, in 108th Congress, S. 15, S. 1504, and H.R. 2122 (The Project BioShield Act of 2003, Sen. Judd and Rep. Tauzin) would guarantee a government market for certain biomedical countermeasures against potential bioterror agents and S. 666 (the Biological, Chemical, and Radiological Weapons Countermeasures Research Act, Sen. Lieberman) would provide tax and market based incentives to encourage companies to develop treatments for bioterror agents.

¹³⁸ For example see, Greg Seigle, "Feds Could Make Bioterror 'Impossible', Expert Says," *Global Security Newswire*, April 9, 2002.

Separating Assessments of Chemical and Biological Agents

The concept of WMD, while useful in a military framework, may obscure some dangers of a terrorist threat. Policymakers may want to consider whether continuing attempts to treat all non-conventional weapons within the same framework is adequate for the terrorist threat. An alternative is to treat the different threats in separate frameworks.

Methods for controlling proliferation and production of C/B agents are often assumed to be equally applicable to both types of agents. Policymakers may want to determine whether it is valid to regulate biological (including toxins) and chemical agents jointly. Since inhibition of C/B proliferation involves similar issues, namely large volumes of dual-use machinery, a similar educational and financial component, and a sliding production scale, a combined regulatory approach may be a reasonable solution. It may provide for clear, uniform standards, and simplify the regulatory process.

Alternatively, policymakers may wish to regulate chemical and biological agents separately, focusing on areas where they differ technically. For example, biological agents lack signatures which can be detected from a distance, while chemical agents have signatures unique to these agents; laser remote sensing has been used to determine if clouds contain nerve agents. Detecting biological agents requires sensitive, agent-specific detectors, and this difficulty in detecting biological agents complicates remote monitoring of potential biological agent laboratories. Also, since most biological agents, unlike most chemical agents, are available in nature, preventing access to seed stocks of biological material is more difficult than blocking access to chemical precursors. Detection methods for biological agents need to be able to differentiate between naturally occurring and anthropogenic pathogens.¹³⁹ For example, to find a hidden terrorist anthrax laboratory, a sensor would need to distinguish between the background, naturally occurring levels of anthrax spores and those coming from the covert facility.¹⁴⁰ Creating regulations addressing chemical and biological agents in separate frameworks may provide a more rigorous control of these agents.

Acceptable Level of C/B Terrorism Risk

A further issue policymakers may consider is how to balance an acceptable degree of risk from C/B terrorism against the amount of security required to address this risk. Viewed from a statutory and regulatory perspective, the C/B terrorism risk appears to be reduced from the 2001 level. Current laws limit access to, record

¹³⁹ See CRS Report RL32152 *The BioWatch Program: Detection of Bioterrorism* by Dana A. Shea and Sarah A. Lister.

¹⁴⁰ U. S. forces in Afghanistan reportedly have found traces of anthrax at several al Qaeda sites, but have been unable to determine its origin. Niles Latham, "Al Qaeda Lab Hunt Reveals Anthrax," *The New York Post*, March 26, 2002.

possession of, and limit the transfer of pathogens on the Select Agent list.¹⁴¹ Congress has allocated funding to improve aspects of the public health system, including research into agent detectors and epidemiological surveillance, to reduce the vulnerability level. Increased law enforcement efforts designed to reduce the general terrorist threat also reduce the probability of a C/B terror attack. There appears to be a concerted attempt to significantly lower the risk of C/B terrorism.

A complete removal of domestic C/B vulnerability is probably impossible. A maximum effort would likely require, among other measures, in-depth searches of all materials entering the country, strict purchasing controls on all dual-use technologies, and industrial controls, such as registration, increased security procedures, and regular inspection of sites engaged in chemical or biological manufacture. The cost of such a program could be high, both in economic terms and civil liberties. Policymakers may likely consider the balance between further decreasing vulnerability and the continued success of industry and research when crafting additional legislation and regulation.

Advances in Science and Science Policy

Scientific advances may alter some of the conclusions of the above analysis, which addresses naturally occurring strains of pathogens, their natural distribution, and the known methods of treatment for them. It does not, for example, address intentionally induced antibiotic resistance; pathogen strains designed to evade current vaccines; Novichok-type chemical agents;¹⁴² or the expression of toxins from genetically-modified organisms. While all of these items are reportedly possible with current technology, their production requires a greater degree of knowledge and experience than that needed to produce pathogens, chemical agents, and toxins addressed in this report. The successful synthesis of polio virus¹⁴³ and the development of a genetically engineered strain of mousepox highly lethal to even

¹⁴¹ The Antiterrorism and Effective Death Penalty Act of 1996 (P. L. 104-132) requires any institution or person transferring listed agents to register with CDC. The USA PATRIOT Act (P. L. 107-56) places additional limitations on the status of persons who may knowingly possess, transport or receive such agents. The Public Health Security and Bioterrorism Preparedness and Response Act of 2002 (P. L. 107-188) requires registration with the Secretary of Health and Human Services of the possession, use, and transfer of listed agents and toxins.

¹⁴² Novichok-type agents are a reported, though not confirmed, chemical agent type which is created without using any chemicals listed by the verification schedules of the CWC. Novichok-type agents are reported to be more lethal than VX. For more information on Novichok agents, see Vil Mirzayanov, "Dismantling the Soviet/Russian Chemical Weapons Complex: An Insider's View," in *Chemical Weapons Disarmament in Russia: Problems and Prospects*, Washington, D.C.: Henry L. Stimson Center, 1995.

¹⁴³ Jeronimo Cello, Aniko V. Paul, and Eckard Wimmer, "Chemical Synthesis of Poliovirus cDNA: Generation of Infectious Virus in the Absence of Natural Template," *Science* 297 (2002): 1016-1018. See CRS Report RS21369 *Synthetic Poliovirus: Bioterrorism and Science Policy Implications* by Frank Gottron.

vaccinated mice¹⁴⁴ stand as stark examples of how advances in relevant research can potentially change fundamental assumptions underlying an analysis.

Conclusions

This report is designed to provide a framework for legislators to use in developing risk-management-based policies, rather than vulnerability-based policies, to protect against chemical, biological, and toxin attacks. This analysis addresses relatively small-scale attacks that could be accomplished by determined, non-state-sponsored terrorists.

The analysis presented in this report is consistent with the findings of the Gilmore Commission, which stated that preparation against a large-scale chemical or biological attack would not necessarily simultaneously protect against smaller-scale attacks. This analysis suggests that agents that are effective for small-scale attacks are not necessarily the agents of choice for massive-scale attacks. This is in part explained by the higher availability of commercial equipment to prepare, store, and disseminate an agent, and in part explained by the less restrictive safety and logistical requirements of a small attack in comparison to a large attack. Small attacks require amounts of equipment and supplies that are less likely to trigger regulatory notice. The presence of dual-use equipment in industrial settings may mean that obtaining the required technology for C/B production may be less difficult than previously thought.

Another potential use for this analysis is to determine a possible priority with which the threat presented by specific agents should be addressed. This analysis provides information on the general approaches to reduce the threat from terrorist use of different C/B agents, as well as information that may allow policymakers to reduce the dangers from specific agents. The analysis could be useful in decisions related to policy options, such as developing specific remedies (e.g. cures, prophylaxis, detection equipment) and more efficient public health mechanisms for detecting and treating the agents towards the tops of these matrices.

The terrorist attacks of 2001 increased the awareness of the vulnerabilities of the United States to asymmetric attacks. Policymakers are carefully re-examining many policies to reduce the threat of future attacks. Some policies already changed include an increase in public health funding; an increase in C/B related research funding; an increase in regulatory oversight of C/B agents; and greater limitations on access to potential C/B agents. While some steps have been taken towards increasing the robustness of the public health system, how increased funding will translate into greater preparedness for and response to a C/B attack is still an open question.¹⁴⁵

¹⁴⁴ Ronald J. Jackson *et al.*, "Expression of Mouse Interleukin-4 by a Recombinant Ectromelia Virus Suppresses Cytolytic Lymphocyte Responses and Overcomes Genetic Resistance to Mousepox," *Journal of Virology* 75 (2001): 1205-1210.

¹⁴⁵ See CRS Report RL31719 *An Overview of the U.S. Public Health System in the Context of Bioterrorism* by Holly Harvey and Sarah Lister.

Efforts to limit the risk of bioterrorism through greater physical control of certain pathogens have elicited concerns regarding unexpected costs.¹⁴⁶

Other issues that may be of interest to policymakers in the future include limiting access to C/B related scientific data,¹⁴⁷ and increasing electronic and physical surveillance to discover C/B use at an early stage.¹⁴⁸ The Department of Health and Human Services has established a National Science Advisory Board for Biosecurity to aid in determining whether unclassified, federally funded, fundamental research may pose a threat to national security, while the Department of Homeland Security is supporting the BioWatch program for early detection of catastrophic bioterrorism. Whether these programs are successful in addressing the threat posed by C/B terrorism, including small scale C/B terrorism, will likely be an area of congressional interest.

¹⁴⁶ See CRS Report RL31354 *Possible Impacts of Major Counter Terrorism Security Actions on Research, Development, and Higher Education* by Genevieve J. Knezo

¹⁴⁷ See CRS Report RL31695 *Balancing Scientific Publication and National Security Concerns: Issues for Congress* by Dana A. Shea.

¹⁴⁸ For more information about the BioWatch program, see CRS Report RL32152 *The BioWatch Program: Detection of Bioterrorism* by Dana A. Shea and Sarah A. Lister.

Appendix A

Methodology

How Criteria Were Chosen. The matrix approach is derived from that used by the Centers for Disease Control and Prevention (CDC) in prioritizing potential biological terrorism agents.¹⁴⁹ It should be emphasized that there are many different ways to develop an assessment framework for terror agents. The approach taken here is not the only valid approach, and different results may occur if different criteria and weighting systems are chosen. A military assessment, a public health assessment, and an assessment focusing on terrorist use may have different criteria and relative weighting depending on the assumptions and needs of each assessment type.

The CDC assessed biological agents in a public health framework, using criteria appropriate for considering public health response. These criteria included the public health impact, the dissemination potential, public perception, and special public health preparedness needs. This report contains modified criteria to address qualities that terrorist groups planning a small scale attack might consider. For example, a more general criterion than used by the CDC of public health impact was developed for use in this report. As defined for this report, public health impact refers to a more general impact on the health care system, incorporating both casualties and fatalities. This criterion allows, for example, a more direct comparison of agents which are lethal with those that predominantly injure.

In contrast to the CDC approach, this report provides a framework that separates ease in making and disseminating into separate criteria (ease of acquisition and ease of dissemination). Since both acquisition and dissemination may pose a significant barrier to the use of a C/B agent, it was deemed important to separate these two criteria. Additionally, the person-to-person contagiousness of a pathogen was not considered as a distinct category in contrast to the CDC assessment. From a public health perspective, a massive attack using contagious pathogens could quickly overwhelm the surge capacity of the public health system. However, in assessing distribution of such an agent, contagiousness may be considered as making the agents easier to disseminate. Contagion may leverage the dissemination of a pathogen. For example, the initial release may need only to successfully infect a single individual to be effective. This infected individual might now further disseminate the pathogen inadvertently, infecting others. For this reason, this report considers contagion as a positive in terms of ease of dissemination if a pathogen is transmissible through casual contact. In contrast, agents that are contagious only through close contact or by exchange of bodily fluids may be less effective means of dissemination.

This report addresses small-scale terror attacks, and so does not postulate any enhanced requirements for preparation. The number of casualties and fatalities arising from a small-scale attack may have a large public health impact, but the mechanisms already in place to provide rush pharmaceuticals (if available), track and locate affected people, and perform required diagnostics should be sufficient for

¹⁴⁹ Centers for Disease Control and Prevention, "Public Health Assessment of Potential Biological Terrorism Agents," *Emerging Infectious Diseases* 8 (2002): 225.

events of this scale. Consequently, the CDC assessment of special preparation has been reduced to two remaining components, the response to medical treatment of various agents and the pre-event prophylaxis which may be available to the population to ameliorate the impact of the event. These two criteria may have equal weight to a terrorist, as either would reduce the effects of a terror agent dissemination.

The final criterion used in this report is the degree to which various agents have been investigated by military weapons programs. Agents which reportedly have been weaponized or were research targets for a weapons program may be available for purchase or theft by terrorist groups. Additionally, records of the weaponization process, information about successful or unsuccessful research routes, and knowledge of optimized processes for these agents may be available. While there are few data available in the open literature about the level of information available to terrorist groups from these weapons programs, the possibility that there could be technology transfer from a state program to a terrorist group factors into the relative threat analysis. Additionally, the fact that an agent may not be explicitly cited as being part of a weapons program does not preclude its presence in one. Instead, this merely means that it is unknown from open sources whether any weapons-related research has been performed regarding it.

These criteria were originally developed for pathogens, and since this report also considers chemical and toxin agents, the criteria were further adapted for use with toxin and chemical agents. Since the chemical agents considered in this report have been considered as chemical weapons for many years, a chemical agent's status in a weapons program seemed superfluous and was omitted from the assessment. Also, prophylaxis for chemical agents, in general, refers to physical protection comprised of impermeable suits and barriers to personal exposure. Since this report focuses on the threat to an unprepared civilian population, it was considered unlikely that prophylaxis would be available for such a surprise attack. Consequently, this criterion was removed.

The Weighting System.

Between Criteria. In this analysis, each individual criterion is given equal weighting. This was done to imply that each of the criteria can be viewed from a generic perspective of use to have roughly equal importance. As discussed elsewhere in this report, some terrorist groups, because of specific aims, ideology or expertise, may place more importance on some categories than on others. For example, a group with extensive practical experience in dissemination technology may place much less importance on this category than a group lacking this specialized knowledge. By weighting all the criteria equally, this limited analysis attempts to rate the domestic risk of potential terrorist use of these agents to a first approximation. The criteria have been made equivalent in the absence of information requiring a different weighting. Other weighting systems using these data may be useful for other purposes.

Within Criteria. Each criterion was divided into three segments to develop a relative scale of influence. Consequently, a — refers to an aspect that is a negative influence to terrorist use, while a + refers to an aspect that is a positive influence to

terrorist use. The **O** rank represents an intermediate state. For example, in the prophylaxis criterion, a — denotes licensed prophylaxis while a + denotes no prophylaxis at all. A **O** denotes an experimental prophylaxis lacking Food and Drug Administration approval.

In defining the scale within criteria, an effort was made to logically group the range of possibilities into three segments. The separation between segments is more distinct in some categories than in others. Because of the coarseness of this scale, agents that receive the same symbol within a criterion do not necessarily possess the same exact properties, but instead should be considered roughly comparable. The full scale of potential response may not be presented in these categories, as the agents presented here are those agents which have been identified as having the potential to be used as a bioweapon. These agents have, generally, been preselected to possess appropriate characteristics for use. As a consequence, the definitions developed address the characteristics of bioweapons rather than C/B agents in general.

The full spectrum of potential agents is not represented in these matrices. The selection process for agents described in the text requires that potential agents be identified by multiple lists of agents of concern. This process removes many agents which appear to have low terrorism potential and agents not considered a threat to the populace at large. Because of this truncation, there are few examples of very poor C/B agents found on the matrices.

Ranking. Agents were ranked based on the symbols assigned within each criterion. Agents were first sorted by the number of barriers to their successful terrorist use: the incidence of — symbols for a given agent initially determined the ranking of an agent. Agents with equivalent numbers of — symbols were then sorted according to the number of **O** symbols present. In the case of further equivalency, the number of + symbols were considered. If equivalent rankings result, agents which have been successfully weaponized are presented above those which have been research targets. Agents which are fully equivalent in ranking and weaponization status are presented in alphabetical order.

Agents are presented in the matrices in inverse order to the number of barriers to their successful terrorist use. Thus, agents which possess the greatest number of barriers are presented at the bottom of the matrix. Agents with equivalent ranking are presented grouped together within the matrices. This type of analysis is not designed to produce a highly differentiated ranking of agents, but a qualitative understanding of relative dangers. Therefore, this list does not attempt to discriminate agents of roughly equal ranking.

The sorting mechanism used here is not the only mechanism which might be applied to this framework, but it was felt that sorting according to the number of barriers would more properly address criteria which might block successful use of a given agent. This implies that a terrorist may use an agent which is less well-suited, but lacks significant barriers, rather than an highly effective agent, which has a significant barrier to its use. Further refinement of the range of characteristics involved in a given symbol or criterion or reranking agents using other methods may lead to a different assessment of each agent and its relative threat. For example,

some may wish to sort this framework according to positive factors. This changes the order of some agents, although the overall ordering of the matrix remains similar.

Appendix B

Table 4. Comparison of chemical agent characteristics

Chemical Agent	Ease of Acquisition	Public Health Impact	Resistance to Medical Treatment	Ease of Dissemination
Nitrogen Mustard ^a	Nitrogen mustard has been used as a chemotherapy agent. Its synthesis produces few toxic byproducts and is not technically complex.	Exposure to nitrogen mustard produces effects similar to sulfur mustard. Skin exposure causes blistering, while inhalation causes severe airway damage. The lethal concentration over time which will kill 50% of those exposed ($LC_{t_{50}}$) is 1,500 (milligrams * minutes) per meter ³ [or (mg*min)/m ³]. The lethal dosage which will kill 50% of those exposed (LD_{50}) is 10 mg per kilogram (or mg/kg). (See Table Note).	Other than supportive care, there is no specific treatment for nitrogen mustard exposure.	Nitrogen mustard is both a vapor and a liquid threat to skin and lungs.
Sulfur Mustard ^b	Sulfur mustard was first synthesized in the early 1800s. Its synthesis produces few toxic byproducts and is not technically complex. It has no commercial uses.	Skin exposure to sulfur mustard causes blisters on the skin several hours after exposure. Inhalation of sulfur mustard causes severe airway damage. Exposure to large amounts of sulfur mustard by either method causes gastrointestinal and bone marrow damage. The $LC_{t_{50}}$ is 1,500 (mg * min)/m ³ . The LD_{50} is 100 mg/kg. Amounts as small as 10 microgram (mcg) will cause blistering.	Other than supportive care, there is no specific treatment for sulfur mustard exposure.	Sulfur mustard is both a vapor and a liquid threat to skin and lungs.
Phosgene Oxime ^c	Phosgene oxime has no industrial use. Its synthesis generates significant toxic side products.	Skin exposure to phosgene oxime vapor results in immediate burning and pain, followed by wheal-like skin lesions. Inhalation causes severe pulmonary edema. The extreme pain from phosgene oxime exposure may persist for days. The $LC_{t_{50}}$ is 3,200 (mg * min)/m ³ . The LD_{50} is 25 mg/kg.	Other than supportive care, there is no specific treatment for phosgene oxime exposure.	Phosgene oxime is a solid, but the vapor pressure of the solid is high enough to make it a contact and inhalation threat.

Chemical Agent	Ease of Acquisition	Public Health Impact	Resistance to Medical Treatment	Ease of Dissemination
Lewisite ^d	Lewisite has no industrial use. Its synthesis has significant toxic side products, but is not technically complex.	Skin exposure to Lewisite causes immediate pain and a grayish area of dead skin, followed by blister formation. Lewisite causes more skin damage than mustard. Inhalation of Lewisite causes immediate burning pain, profuse nasal secretions, cough and lung edema. The LCt_{50} is 1,200 (mg * min)/m ³ . The LD_{50} is 40 mg/kg. Amounts as small as 10-15 mcg will cause blistering.	A specific antidote, British-Anti-Lewisite (BAL, dimercaprol), will alleviate some effects of Lewisite, but is no longer in production. Otherwise, treatment is symptom based.	Lewisite is both a vapor and a liquid threat to skin and lungs.
Cyclohexyl Sarin ^e	Cyclohexyl sarin has no industrial use. Its synthesis produces significant toxic side products.	Inhalation exposure to cyclohexyl sarin causes runny nose, pin-point pupils, difficulty breathing, nausea, and muscle seizure. Death usually occurs quickly after absorption of a fatal dosage. The LD_{50} is 30 mg/kg.	Atropine and pralidoxime chloride are recommended for treatment of cyclohexyl sarin exposure. For severe cases, diazepam is given to limit seizures.	Cyclohexyl sarin is a threat by inhalation, and secondarily through skin contact.
Sarin ^f	Sarin has no industrial use. Its synthesis produces significant toxic side products.	Inhalation exposure to sarin causes runny nose, pin-point pupils, difficulty breathing, nausea, and muscle seizure. Death usually occurs quickly after absorption of a fatal dosage. The LCt_{50} is 100 (mg * min)/m ³ . The LD_{50} is 24 mg/kg.	Atropine and pralidoxime chloride are recommended for treatment of sarin exposure. For severe cases, diazepam is given to limit seizures.	Sarin is a threat by inhalation, and secondarily through skin contact.
Tabun ^g	Tabun has no industrial use. Its synthesis produces significant toxic side products.	Inhalation exposure to tabun causes runny nose, pin-point pupils, difficulty breathing, nausea, and muscle seizure. Death usually occurs quickly after absorption of a fatal dosage. The LCt_{50} is 400 (mg * min)/m ³ . The LD_{50} is 14 mg/kg.	Atropine and pralidoxime chloride are recommended for treatment of tabun exposure. For severe cases, diazepam is given to limit seizures.	Tabun is a threat by inhalation, and secondarily through skin contact.

Chemical Agent	Ease of Acquisition	Public Health Impact	Resistance to Medical Treatment	Ease of Dissemination
VX ^b	VX has no industrial use. The synthesis of VX generates lethal side products.	Inhalation exposure to VX causes runny nose, pin-point pupils, difficulty breathing, nausea, and muscle seizure. Death usually occurs quickly after absorption of a fatal dosage. The LD_{50} is 10 (mg * min)/m ³ . The LD_{50} is 140 mcg/kg.	Atropine and pralidoxime chloride are recommended for treatment of VX exposure. For severe cases, diazepam is given to limit seizures.	VX is a threat both by skin contact and inhalation.
Ammonia ⁱ	Ammonia is widely used in industrial processes, including petroleum, pulp and paper, and food and beverage industries.	Exposure to ammonia causes irritation of the eyes, nose and throat. Exposure to large amounts of ammonia causes pulmonary edema. Death is a rare consequence of ammonia exposure.	Other than supportive care, there is no specific treatment for ammonia exposure.	Ammonia is an inhalation threat.
Chlorine ^j	Chlorine is used in varied industrial processes, including water purification, pharmaceutical, and chemical industries.	Chlorine inhalation causes irritation of the eyes, nose and throat, with pulmonary edema and airway swelling and obstruction after exposure to high-concentrations. Death is a rare consequence.	Other than supportive care, there is no specific treatment for chlorine exposure.	Chlorine is an inhalation threat.
Chloropicrin ^k	Chloropicrin is a soil fumigant used for its broad biocidal and fungicidal properties. It is commercially available.	Inhalation of chloropicrin causes coughing, dizziness, bluish skin, vomiting, and pulmonary edema. Contact with chloropicrin can lead to chemical burns or dermatitis. The LCt_{50} is 16,000 (mg * min)/m ³ . The LD_{50} is 250 mg/kg.	Other than supportive care, there is no specific treatment for chloropicrin exposure.	Chloropicrin is a threat both by inhalation and contact.
Phosgene ^l	Phosgene was first synthesized in 1812. It is used in industrial processes, such as dye and plastic manufacturing.	Inhalation of phosgene causes extensive cellular damage to the lung membrane. Victims may suffer cough, and pulmonary edema. Death from phosgene inhalation can occur. The LCt_{50} is 3,200 (mg * min)/m ³ .	Other than supportive care, there is no specific treatment for phosgene exposure.	Phosgene, with its high volatility, is an inhalation threat.

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Chemical Agent	Ease of Acquisition	Public Health Impact	Resistance to Medical Treatment	Ease of Dissemination
Soman ^m	Soman has no industrial use. Its synthesis produces <i>significant</i> toxic side products.	Inhalation exposure to soman causes runny nose, pin-point pupils, difficulty breathing, nausea, and muscle seizure. Death usually occurs quickly after absorption of a fatal dosage. The LC ₅₀ is 50 (mg * min)/m ³ . The LD ₅₀ is 5 mg/kg.	Atropine and pralidoxime chloride are recommended for treatment of soman exposure. Pralidoxime chloride treatment must be given within two minutes of exposure to be effective against soman. For severe cases, diazepam is given to limit seizures.	Soman is a threat by inhalation, and secondarily through skin contact.
Diphosgene ⁿ	Diphosgene has no industrial use. Its synthesis has significant toxic side products.	Diphosgene causes irritation of the respiratory tract and delayed pulmonary edema. The LC ₅₀ is 3000 (mg * min)/m ³ .	Other than supportive care, there is no specific treatment for diphosgene exposure.	Diphosgene, with its high volatility, is an inhalation threat.
Cyanogen Chloride ^o	Cyanogen chloride is used in varied industrial processes, including mining and metalworking.	After inhalation of a high concentration of cyanogen chloride, there is the onset of convulsions, as well as heavy irritation of the eyes and respiratory tract, similar to chlorine exposure. Death occurs as quickly as six to eight minutes. The LC ₅₀ is 11,000 (mg * min)/m ³ .	Sodium nitrite and sodium thiosulfate are effective antidotes in a two-step process. This combination may save those exposed to up to 20 times the lethal dose, and is effective even after breathing has stopped. General supportive care is given if specific antidotal treatment is not available. Several alternative therapies are experimental antidotes used in other countries.	Cyanogen chloride, with its high volatility, is an inhalation threat.

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Chemical Agent	Ease of Acquisition	Public Health Impact	Resistance to Medical Treatment	Ease of Dissemination
Hydrogen Cyanide ^P	Hydrogen cyanide is widely used in industry. The U.S. manufactures over 300,000 tons of hydrogen cyanide annually for use in chemical syntheses, electroplating, mineral extraction, dyeing, printing, photography, paper, textile, and plastic manufacture.	Exposure to a sublethal dose of hydrogen cyanide tends to not cause marked symptoms. After inhalation of a high concentration of hydrogen cyanide, there is the onset of convulsions. Death occurs as quickly as six to eight minutes after exposure. The LCt_{50} is 2,500 - 5,000 (mg min)/m ³ .	Sodium nitrite and sodium thiosulfate are effective antidotes in a two-step process. This combination may save those exposed to up to 20 times the lethal dose, and is effective even after breathing has stopped. General supportive care is given if specific antidotal treatment is not available. Several alternative therapies are experimental antidotes used in other countries.	Hydrogen cyanide, with its high volatility, is an inhalation threat.
Perfluoroisobutylene ^Q	Perfluoroisobutylene was used as an industrial chemical, but is no longer manufactured due to its toxicity.	Inhalation of perfluoroisobutylene causes a rapid toxic effect on pulmonary tissues. Edema occurs within 5 minutes. Cough productive of bloody sputum occasionally is seen. Death is a rare consequence of exposure.	Other than supportive care, there is no specific treatment for perfluoroisobutylene exposure.	Perfluoroisobutylene is an inhalation threat.

Source: These data were prepared by the authors from the open literature.

Note: The LD_{50} is the dosage of agent per unit body weight required to kill 50% of those exposed. It is expressed here in micrograms (mcg) per kilogram (kg). A microgram weighs approximately as much as the ink used to print a single character on this sheet of paper. A 155 lb. person weighs approximately 70 kilograms. The LCt_{50} is the concentration of chemical agent lethal over time to 50% of those exposed. It is expressed in units of (mg * min)/m³. LD_{50} values commonly refer to liquid exposure, while LCt_{50} commonly refer to gaseous exposure.

- ^a Information on nitrogen mustard is taken from “Vesicants,” by Frederick R. Sidell *et al.*, in *Medical Aspects of Chemical and Biological Warfare*, eds. Frederick R. Sidell, Ernest T. Takafuji, and David R. Franz, Washington, DC: TMM Publications, 1997; D. Hank Ellison, *Handbook of Chemical and Biological Warfare Agents*, Boca Raton, FL: CRC Press, 2000; Frederick R. Sidell, William C. Patrick, III, and Thomas R. Dashiell, *Jane’s Chem-Bio Handbook*, Alexandria, VA: Jane’s Information Group, 1998; and the Federation of American Scientists Special Weapons Primer, found online at [<http://www.fas.org/nuke/intro/cw/index.html>].
- ^b Information on sulfur mustard is taken from the U.S. Army, *Medical Management of Chemical Casualties Handbook*, Medical Research Institute of Chemical Defense Chemical Casualty Care Division, Aberdeen, MD, 1999; Frederick R. Sidell, *et al.* “Vesicants,” *Medical Aspects of Chemical and Biological Warfare*, *op. cit.*; and Frederick R. Sidell, William C. Patrick, III, and Thomas R. Dashiell, *Jane’s Chem-Bio Handbook*, *op. cit.*
- ^c Information on phosgene oxime is taken from U.S. Army, *Medical Management of Chemical Casualties Handbook*, *op. cit.*; Frederick R. Sidell, *et al.* “Vesicants,” *Medical Aspects of Chemical and Biological Warfare*, *op. cit.*; and Frederick R. Sidell, William C. Patrick, III, and Thomas R. Dashiell, *Jane’s Chem-Bio Handbook*, *op. cit.*
- ^d Information on lewisite is taken from the Agency for Toxic Substances & Disease Registry, “*Medical Management Guidelines — Blister Agents*,” Centers for Disease Control and Prevention, Washington DC; Frederick R. Sidell, *et al.* “Vesicants,” *Medical Aspects of Chemical and Biological Warfare*, *op. cit.*; Frederick R. Sidell, William C. Patrick, III, and Thomas R. Dashiell, *Jane’s Chem-Bio Handbook*, *op. cit.*; and the U.S. Army, *Medical Management of Chemical Casualties Handbook*, *op. cit.*
- ^e Information on cyclohexyl sarin is taken from the U.S. Army, *Medical Management of Chemical Casualties Handbook*, *op. cit.* and “Nerve Agents,” by Frederick R. Sidell, *Medical Aspects of Chemical and Biological Warfare*, *op. cit.*
- ^f Information on sarin is taken from the U.S. Army, *Medical Management of Chemical Casualties Handbook*, *op. cit.*; “Nerve Agents,” by Frederick R. Sidell, *Medical Aspects of Chemical and Biological Warfare*, *op. cit.*; and Frederick R. Sidell, William C. Patrick, III, and Thomas R. Dashiell, *Jane’s Chem-Bio Handbook*, *op. cit.*
- ^g Information on tabun is taken from the Agency for Toxic Substances & Disease Registry, “*Medical Management Guidelines — Nerve Agents*,” *op. cit.*; “Nerve Agents,” by Frederick R. Sidell, *Medical Aspects of Chemical and Biological Warfare*, *op. cit.*; and Frederick R. Sidell, William C. Patrick, III, and Thomas R. Dashiell, *Jane’s Chem-Bio Handbook*, *op. cit.*; the U.S. Army, *Medical Management of Chemical Casualties Handbook*, *op. cit.*
- ^h Information on VX is taken from the Agency for Toxic Substances & Disease Registry, “*Medical Management Guidelines — Nerve Agents*,” *op. cit.*; “Nerve Agents,” by Frederick R. Sidell, *Medical Aspects of Chemical and Biological Warfare*, *op. cit.*; and Frederick R. Sidell, William C. Patrick, III, and Thomas R. Dashiell, *Jane’s Chem-Bio Handbook*, *op. cit.*; the U.S. Army, *Medical Management of Chemical Casualties Handbook*, *op. cit.*
- ⁱ Information on ammonia is taken from the Agency for Toxic Substances & Disease Registry, “*Medical Management Guidelines — Ammonia*,” *op. cit.* and “Toxicity, Ammonia,” by Steven Issley and Eddy Lang, eMedicine Knowledge base, found online at [<http://www.emedicine.com/EMERG/topic846.htm>].
- ^j Information on chlorine is taken from the Agency for Toxic Substances & Disease Registry, “*Medical Management Guidelines — Chlorine*,” *op. cit.* “CBRNE - Lung-Damaging Agents, Chlorine,” by Daniel Noltkamper and Gerald F. O’Malley, eMedicine Knowledge base, found online at [<http://www.emedicine.com/EMERG/topic904.htm>].
- ^k Information on chloropicrin is taken from “CBRNE - Lung-Damaging Agents, Chloropicrin,” by Joanne Williams, eMedicine Knowledge base, found online at [<http://www.emedicine.com/emerg/topic907.htm>]; the Fisher Scientific Material Safety Data Sheet for Chloropicrin; and the National Institutes of Health National Toxicology Program fact sheet for chloropicrin.
- ^l Information on phosgene is taken from *Strategies to Protect the Health of Deployed U.S. Forces: Detecting, Characterizing, and Documenting Exposures*, eds. Thomas E. McKone, *et al.*, Washington, D.C.: National Academy Press, 2000; Agency for Toxic Substances & Disease Registry, “Medical Management Guidelines — Phosgene,” *op. cit.*; and “CBRNE - Lung-Damaging Agents, Phosgene,” by Jeffrey L. Arnold, eMedicine Knowledge base, found online at [<http://www.emedicine.com/EMERG/topic905.htm>].
- ^m Information on soman is taken from the Agency for Toxic Substances & Disease Registry, “*Medical Management Guidelines — Nerve Agents*,” *op. cit.*; “Nerve Agents,” by Frederick R. Sidell, *Medical Aspects of Chemical and Biological Warfare*, *op. cit.*; Frederick R. Sidell, William C. Patrick, III, and Thomas R. Dashiell, *Jane’s Chem-Bio Handbook*, *op. cit.*; the U.S. Army, *Medical Management of Chemical Casualties Handbook*, *op. cit.*; and “CBRNE - Chemical Warfare Agents,” by Jeffrey L. Arnold, eMedicine Knowledge base, found online at [<http://www.emedicine.com/EMERG/topic852.htm>].
- ⁿ Information on diphosgene is taken from *Strategies to Protect the Health of Deployed U.S. Forces: Detecting, Characterizing, and Documenting Exposures*, *op. cit.* and “CBRNE - Lung-Damaging Agents, Diphosgene,” by Eric Mowatt-Larsen and Paul P. Rega, eMedicine Knowledge base, found online at [<http://www.emedicine.com/emerg/topic906.htm>]

- ° Information on cyanogen chloride is taken from the U.S. Army, *Medical Management of Chemical Casualties Handbook*, *op. cit.*; Frederick R. Sidell, William C. Patrick, III, and Thomas R. Dashiell, *Jane's Chem-Bio Handbook*, *op. cit.*; Steven I. Baskin and Thomas G. Brewer, "Cyanide Poisoning," in *Medical Aspects of Chemical and Biological Warfare*, *op. cit.*; and "CBRNE - Cyanides, Cyanogen Chloride," by Heather Murphy-Lavoie, eMedicine Knowledge base, found online at [<http://www.emedicine.com/emerg/topic910.htm>].
- ° Information on hydrogen cyanide is taken from U.S. Army, *Medical Management of Chemical Casualties Handbook*, *op. cit.*; Frederick R. Sidell, William C. Patrick, III, and Thomas R. Dashiell, *Jane's Chem-Bio Handbook*, *op. cit.*; Steven I. Baskin and Thomas G. Brewer, "Cyanide Poisoning," in *Medical Aspects of Chemical and Biological Warfare*, *op. cit.*
- ° Information on perfluoroisobutylene is taken from John S. Urbanetti, "Toxic Inhalational Injury," in *Medical Aspects of Chemical and Biological Warfare*, *op. cit.* and "CBRNE - Lung-Damaging Agents, Toxic Smokes: Nox, Hc, Rp, Fs, Fm, Sgf2, Teflon," by Daniel T. Smith and Andrea M. DuPont, eMedicine Knowledge base, found online at [<http://www.emedicine.com/emerg/topic908.htm>].

Appendix C

Table 5. Comparison of biological agent characteristics

Disease (Biological Agent)	Ease of Acquisition	Public Health Impact	Prophylaxis	Resistance to Medical Treatment	Ease of Dissemination
Glanders ^a (<i>Burkholderia mallei</i>)	<i>Burkholderia mallei</i> is endemic in a number of species including horses, dogs and sheep in Africa, Asia, the Middle East, and Central and South America.	In pulmonary infections, pneumonia, pulmonary abscesses, and pleural effusion can occur. The fatality rate is over 50% even with treatment. Skin lesions and ulcers occur from the contact form of glanders.	There is no vaccine for glanders.	Because of the rarity of human infection, the response to many antibiotics is not known.	Glanders could be disseminated via aerosol or through contaminated food or drink.
Crimean-Congo hemorrhagic fever ^b	Crimean-Congo hemorrhagic fever has been observed in western Crimea, Central Asia, the Balkan region, Iraq, the Arabian Peninsula, western China, tropical Africa and South Africa. Recent well publicized outbreaks have occurred on the Iran — Pakistan border. Several bird and rodent species serve as hosts.	Crimean-Congo hemorrhagic fever causes malaise, weakness, irritability, headache, severe pain, and marked anorexia. Vomiting, and diarrhea may also occur. In severe cases, bleeding from the gums, nose, lungs, and intestine can occur, leading to death due to loss of blood. The case fatality rate is approximately 30%.	There is no vaccine for Crimean- Congo hemorrhagic fever.	Specific treatment with the anti-viral drug, ribavirin may be effective if promptly given.	Crimean- Congo hemorrhagic fever could be disseminated via aerosol. It is contagious through close contact.

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Disease (Biological Agent)	Ease of Acquisition	Public Health Impact	Prophylaxis	Resistance to Medical Treatment	Ease of Dissemination
Pneumonic Plague ^c (<i>Yersinia pestis</i>)	<i>Yersinia pestis</i> , the causative agent of both bubonic and pneumonic plague, is found world wide, with several animal reservoirs. Cases of plague, usually in bubonic rather than pneumonic form, occur in the United States each year. Large plague outbreaks occur less frequently, but are more widely reported.	Pneumonic plague causes fever, headache, weakness, and rapidly developing pneumonia with shortness of breath, chest pain, and cough. The pneumonia progresses for 2 to four days and may cause respiratory failure and shock. Without early treatment, 90% of the patients die.	There is no publicly available vaccine for plague in the United States, although several have IND status.	Plague can often be treated with antibiotics, but only if given in the first 24 hours.	Pneumonic plague could be disseminated via aerosol. It is contagious through casual person-to-person contact.
Hantavirus ^d	Hantavirus is found in nature, with rodents as a natural reservoir within the United States. Outbreaks of hantavirus are widely reported in the media	Hantavirus can cause either hantavirus pulmonary syndrome or a hemorrhagic fever with renal syndrome. Hantavirus pulmonary syndrome consists of fever, fatigue, muscle aches, coughing and shortness of breath. In advanced cases, heavy pulmonary edema occurs. The fatality rate for hantavirus pulmonary syndrome is 37%. Hemorrhagic fever with renal syndrome has a fatality rate of 10%.	There is no vaccine for hantavirus.	Specific treatment with the anti-viral drug, ribavirin may be effective if promptly given.	Hantavirus could be disseminated via aerosol.

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Disease (Biological Agent)	Ease of Acquisition	Public Health Impact	Prophylaxis	Resistance to Medical Treatment	Ease of Dissemination
Dengue hemorrhagic fever ^c	Although dengue fever is endemic in most regions of the tropics, causing epidemic outbreaks among humans, dengue hemorrhagic fever is one of the less common virus strains and would be more difficult to acquire.	Dengue hemorrhagic fever causes a sudden onset of fever, severe headache, muscle pain, and hemorrhagic manifestations. The fatality rate of dengue hemorrhagic fever is about 5%.	There is no licensed vaccine for dengue hemorrhagic fever. Several unlicensed vaccines are under testing.	Other than supportive care, there is no specific treatment for dengue hemorrhagic fever.	Dengue hemorrhagic fever could be disseminated by insect vector.
Eastern equine encephalitis ^f	Eastern equine encephalitis is endemic to the United States. It most commonly occurs east of the Mississippi.	Symptoms range from mild flu-like illness to encephalitis, coma and death. The average duration of hospitalization is 16-20 days. 50-70% of patients die within a few days. Only 10% of patients fully recover. 200 human cases have been confirmed in the U.S. since 1964.	There is no licensed vaccine for human use. Several IND vaccines exist.	Other than supportive care, there is no specific treatment for eastern equine encephalitis.	Eastern equine encephalitis could be disseminated by insect vector or via aerosol.
Lassa fever ^g	Lassa fever is endemic in Guinea, Liberia, Sierra Leone and regions of Nigeria. It has a reservoir in the mouse and rat population.	Lassa fever causes fever, malaise, headache, sore throat, cough, nausea, vomiting, diarrhea, and muscle pain. In severe cases, shock, hemorrhage, seizures, and encephalopathy are frequent. Lassa fever has a fatality rate of 1%.	There is no licensed vaccine for lassa fever.	Specific treatment with the anti-viral drug, ribavirin may be effective if given within the first six days of illness.	Lassa fever could be disseminated via aerosol. It is contagious through close contact.

Disease (Biological Agent)	Ease of Acquisition	Public Health Impact	Prophylaxis	Resistance to Medical Treatment	Ease of Dissemination
Russian spring-summer encephalitis ^h	Russian spring-summer encephalitis, occurs in China, Korea, Japan, and eastern areas of Russia.	Russian spring-summer encephalitis causes a flu-like illness, including fever, headache, vomiting, and neurologic symptoms. Neurologic damage may be permanent, causing chronic headaches, difficulty concentrating, muscle weakness or loss of balance. A small percentage of cases are fatal.	There is no licensed vaccine available in the United States, but some effective vaccines are available in Europe.	There is no specific treatments for Russian spring-summer encephalitis. Supportive care is provided.	Russian spring-summer encephalitis could be disseminated either by tick vector or via aerosol.
Western equine encephalitis ⁱ	Western equine encephalitis occurs within the United States. It is endemic in some states west of the Mississippi River and in the corresponding Canadian provinces. Birds are a natural reservoir for the virus.	Symptoms consists of fever, headache, chills, nausea, and vomiting. The morbidity of such illnesses is higher in infants than in adults. The fatality rate is 3-4%. 639 human cases have been confirmed in the U.S. since 1964.	There is no licensed vaccine for western equine encephalitis. Several IND vaccines exist.	Other than supportive care, there is no specific treatment for Western equine encephalitis.	Western equine encephalitis could be disseminated by insect vector or via aerosol.

Disease (Biological Agent)	Ease of Acquisition	Public Health Impact	Prophylaxis	Resistance to Medical Treatment	Ease of Dissemination
Rift Valley fever ^j	Rift Valley fever is generally found in regions of eastern and southern Africa, but the virus also exists in most countries of sub-Saharan Africa and in Madagascar.	People with Rift Valley fever typically have either no symptoms or a mild illness associated with fever. Some victims progress to hemorrhagic fever. These victims experience fever, generalized weakness, back pain, dizziness, and extreme weight loss at the onset of the illness. The fatality rate of Rift Valley fever is 1%.	An experimental, unlicensed Rift Valley fever vaccine has been developed for human use, but is not commercially available. Other candidate vaccines are under investigation.	Specific treatment with the anti-viral drug, ribavirin may be effective if promptly given.	Rift Valley fever could be disseminated either by insect vector or via aerosol.
Marburg hemorrhagic fever ^k	Recorded cases of the disease are rare, and have appeared in only a few locations. Primary locations of virus sources are in Africa. Sporadic cases occur in that region.	Marburg hemorrhagic fever causes fever, chills, headache, nausea, vomiting, chest and abdominal pain, and diarrhea. Symptoms become increasingly severe and may include delirium, shock, liver failure, massive hemorrhaging, and multi-organ dysfunction. Hospitalization is required. Recovery from Marburg hemorrhagic fever may be prolonged and accompanied by serious complications. The fatality rate for treated Marburg hemorrhagic fever is between 23-25%.	There is no vaccine against Marburg virus.	Other than supportive care, there is no specific treatment for Marburg hemorrhagic fever.	Marburg virus could be disseminated via aerosol. It is contagious through close contact.

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Disease (Biological Agent)	Ease of Acquisition	Public Health Impact	Prophylaxis	Resistance to Medical Treatment	Ease of Dissemination
Ebola hemorrhagic fever ¹	Ebola virus is not widely available. Ebola occurs in nature in parts of Africa, but the vector of infection is unknown, and the barrier to successful collection is likely to be high.	Ebola hemorrhagic fever causes fever, headache, joint and muscle aches, sore throat, and weakness, followed by diarrhea, vomiting, and stomach pain. A rash, red eyes, hiccups, and internal and external bleeding may be seen in some patients. Ebola hemorrhagic fever has a 50 - 90% fatality rate.	There is no vaccine for Ebola virus.	Ebola hemorrhagic fever has no specific treatment. Supportive care is provided.	Ebola hemorrhagic fever could be disseminated via aerosol. It is contagious through close contact.
Melioidosis ^m (<i>Burkholderia pseudomallei</i>)	<i>Burkholderia pseudomallei</i> thrive in tropical climates, and the disease is endemic in Southeast Asia and northern Australia. Naturally occurring outbreaks have been observed in Africa, the Middle East, and Central and South America.	Pulmonary melioidosis is accompanied by a high fever, chest pain, and cough. Pneumonia and pulmonary abscesses occur, leading to death. Fatalities occur in 10% of naturally occurring cases.	There is no vaccine for melioidosis.	Melioidosis can often be successfully treated with long term antibiotic treatment regimens.	Melioidosis could be disseminated via aerosol or through contaminated food or drink.

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Disease (Biological Agent)	Ease of Acquisition	Public Health Impact	Prophylaxis	Resistance to Medical Treatment	Ease of Dissemination
Yellow fever ⁿ	Yellow fever is endemic in some tropical areas of Africa and the Americas, and causes regular epidemics. There are 200,000 estimated cases of yellow fever per year reported worldwide.	Yellow fever causes fever, muscle pain, headache, shivers, loss of appetite, nausea and/or vomiting. 15% of the infected enter a "toxic phase" within 24 hours, which requires hospitalization, as massive bleeding can occur, and kidney function deteriorates. Half of the patients in the "toxic phase" die within 10-14 days. Yellow fever has 8-10% fatality rate.	There is a widely available, tested vaccine against yellow fever.	Other than supportive care, there is no specific treatment for yellow fever.	Yellow fever could be disseminated by insect vector or via aerosol.
Anthrax ^o (<i>Bacillus anthracis</i>)	Anthrax is available both in nature and through a number of culture collections. Anthrax is found in spore form in the soil and causes illness among animals regularly. Numerous anthrax strains, of varying toxicity, exist.	Anthrax has a 1-7 day incubation period. Onset of severe symptoms occurs within 2-5 days of incubation. Hospitalization is often required for those showing disease symptoms. Unvaccinated, untreated individuals with inhalation anthrax suffer up to 90% fatalities.	An anthrax vaccine is available in limited quantities.	Anthrax responds well to combination antibiotic therapy. The recovery rate is ~70% if antibiotic treatment is started early.	Anthrax could be disseminated via aerosol.

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Disease (Biological Agent)	Ease of Acquisition	Public Health Impact	Prophylaxis	Resistance to Medical Treatment	Ease of Dissemination
Q fever ^P (<i>Coxiella burnetii</i>)	<i>Coxiella burnetii</i> is found worldwide. Cattle, sheep, and goats are the primary animal reservoirs of <i>C. burnetii</i> .	Q fever causes sudden onset of high fever, severe headache, pain, confusion, chills, sweats, cough, nausea, vomiting, and/or diarrhea. Fever usually lasts for 1 to two weeks. 30 - 50% of patients with a symptomatic infection will develop pneumonia. Many patients may recover to good health within several months without any treatment. Only 1%-2% of people with acute Q fever die of the disease.	An IND vaccine for Q fever is available from USAMRIID. Australia also has an effective vaccine, which is unavailable in the United States.	Acute and chronic Q fever can often be treated with antibiotics. Q fever is resistant to many antibiotics.	Q fever could be disseminated via aerosol.
Machupo hemorrhagic fever ^Q	Machupo virus is found in remote areas of Bolivia.	Machupo hemorrhagic fever causes fever, malaise, headache, and muscle pains. Bleeding may occur from the nose, gums, stomach, and intestine. The fatality rate is 5-30%.	There is no licensed vaccine for Machupo virus.	Specific treatment with the anti-viral drug, ribavirin may be effective if promptly given.	Machupo hemorrhagic fever could be disseminated via aerosol. It is contagious through close contact.

Disease (Biological Agent)	Ease of Acquisition	Public Health Impact	Prophylaxis	Resistance to Medical Treatment	Ease of Dissemination
Tularemia ¹ (<i>Francisella tularensis</i>)	Tularemia is found in many countries including the United States. <i>Francisella tularensis</i> is a hardy non-spore forming organism that is capable of surviving for weeks at low temperatures in water, moist soil, hay, straw or decaying animal carcasses.	Pulmonary tularemia causes respiratory failure, shock and death. The mortality rate for pulmonary or septicemic cases of tularemia without antibiotics treatment has been as high as 30-60%. With treatment, the fatality rate in the United States is 2%. Between 1990 and 2000, a total of 1,368 human cases of tularemia were diagnosed in the U.S.	An IND vaccine of live, attenuated organisms has been used to prevent laboratory infections.	Tularemia is treated with antibiotics.	Tularemia could be disseminated via aerosol.
Junin hemorrhagic fever ²	Junin virus, is found in a small area of Argentina.	Symptoms are similar to Machupo hemorrhagic fever. Junin has a fatality rate of 5-30%.	There is no licensed vaccine for Junin virus. There is an unlicensed vaccine under testing.	Specific treatment with the anti-viral drug, ribavirin may be effective if promptly given.	Junin virus could be disseminated via aerosol. It is contagious through close contact.
Venezuelan equine encephalitis ³	Venezuelan equine encephalitis is endemic in northern South America, Trinidad, Central America, Florida, and Mexico.	Venezuelan equine encephalitis causes malaise, spiking fevers, severe headache, photophobia, and muscle pains. Nausea, vomiting, cough, sore throat, and diarrhea may follow. Full recovery takes 1-2 weeks. The fatality rate is less than 1%. Nearly 100% of those infected suffer an overt illness.	An IND vaccine, designated TC-83, is a live, attenuated organism vaccine which has been used to prevent laboratory infections.	Other than supportive care, there is no specific treatment for Venezuelan equine encephalitis.	Venezuelan equine encephalitis could be disseminated either by insect vector or via aerosol.

Disease (Biological Agent)	Ease of Acquisition	Public Health Impact	Prophylaxis	Resistance to Medical Treatment	Ease of Dissemination
Typhus ^u (<i>Rickettsia prowazekii</i>)	Epidemic typhus is common during periods when normal hygiene is extremely disrupted, as in refugee camps, war, or natural disasters.	Typhus causes headaches, chills, prostration, high fever, coughing and severe muscular pain. A dark rash spreads to the entire body excepting, usually, the face, palms and soles of the feet. The fatality rate is between 1% and 20%.	There is no licensed vaccine for typhus fever. Several unlicensed experimental vaccines exist.	Typhus is treated with antibiotics.	Typhus could be disseminated either by insect vector or via aerosol.
Rocky Mountain spotted fever ^v (<i>Rickettsia rickettsiae</i>)	Naturally occurring Rocky Mountain spotted fever is the most common potentially fatal tick borne disease in the United States, accounting for between 600 - 800 infections per year.	Rocky Mountain spotted fever can cause fever, rash, headache, muscle pain, nausea, vomiting, confusion, lethargy, seizures and coma. Rocky Mountain spotted fever has a fatality rate of 4%.	An experimental Rocky Mountain spotted fever vaccine is available.	Rocky Mountain spotted fever can be successfully treated with antibiotics.	Rocky Mountain spotted fever could be disseminated either by insect vector or via aerosol.
<i>Escherichia coli</i> O157:H7 ^w	Enterohaemorrhagic <i>E. coli</i> are found in animal reservoirs both within and outside of the United States. Outbreaks of food poisoning related to this <i>E. coli</i> strain are well publicized.	<i>E. coli</i> O157:H7 causes abdominal cramps and watery diarrhea that can develop into bloody diarrhea. Fever and vomiting may occur but most patients recover within 10 days. The fatality rate is less than 1%.	There is no vaccine for <i>E. coli</i> O157:H7.	Other than supportive care, there is no specific treatment for <i>E. coli</i> O157:H7.	<i>E. coli</i> could be disseminated by contamination of food or drink.

Disease (Biological Agent)	Ease of Acquisition	Public Health Impact	Prophylaxis	Resistance to Medical Treatment	Ease of Dissemination
Smallpox ^x (<i>Variola major</i>)	Only two acknowledged sources of <i>Variola major</i> exist, both in controlled facilities, one in Russia, one in the United States.	Smallpox is recognizable by a widespread, full body rash. Treated smallpox has a greater than 30% fatality rate among unvaccinated populations.	There is an effective vaccine against <i>Variola major</i> . The U.S. vaccination program ended in 1972. Previously vaccinated individuals may retain some residual protection.	Vaccine given within 72 hours of exposure reduces disease severity. There is no other treatment for smallpox.	Smallpox could be disseminated via aerosol. It is contagious through casual person-to-person contact.
Monkeypox ^y	Monkeypox occurs in sporadic outbreaks in Africa. Squirrels appear to be a reservoir for the virus.	Symptoms consist of rash and lesions similar to that of smallpox. Monkeypox has a fatality rate of 10%.	The smallpox vaccine protects against monkeypox.	Vaccine given within 72 hours of exposure reduces disease severity. There is no other treatment for monkeypox.	Monkeypox could be disseminated via aerosol. It is contagious through person-to-person contact.
Brucellosis ^z (<i>Brucella abortus</i> , <i>B. melitensis</i> , <i>B. suis</i>)	Brucellosis is found worldwide, and is endemic in the Western United States.	Brucellosis causes fever, sweats, malaise, loss of appetite, headache, and muscle pain. Neurologic symptoms may occur in up to 5% of cases. The fatality rate is less than 2%.	There is no licensed vaccine for brucellosis. Experimental vaccines exist.	Brucellosis can be successfully treated with antibiotics. Treatment regimens usually take from a few weeks to several months.	Brucellosis could be disseminated by contamination of food or drink.

Disease (Biological Agent)	Ease of Acquisition	Public Health Impact	Prophylaxis	Resistance to Medical Treatment	Ease of Dissemination
<i>Shigella dysenteriae</i> ^{aa}	<i>Shigella dysenteriae</i> is endemic in tropical and temperate climates.	Shigellosis is an acute intestinal disease, which causes diarrhea, fever, nausea, vomiting, and cramps. Shigellosis has a 5 - 15% fatality rate when caused by <i>Shigella dysenteriae</i> .	There is no vaccine for <i>Shigella dysenteriae</i> .	Severe shigellosis can usually be treated with antibiotics. Rehydration is necessary for those made ill.	<i>Shigella dysenteriae</i> could be disseminated by contamination of food or drink.
Cholera ^{bb} (<i>Vibrio cholerae</i>)	Cholera occurs in many of the developing countries of Africa and Asia, especially where sanitary conditions are not optimal. Cholera outbreaks have also occurred in parts of Latin America.	Most infected persons have no symptoms or only mild diarrhea. However, persons with severe disease can die within a few hours after onset due to loss of fluid and salts through profuse diarrhea and, to a lesser extent, through vomiting.	There is discontinued, licensed cholera vaccine in the United States. Other vaccines for cholera are licensed and available in other countries.	Cholera is treated with antibiotics to decrease the duration of illness. Supportive treatment involves rehydration. Antibiotic treatment is not necessary to cure the disease.	Cholera could be disseminated via aerosol or through contaminated food or drink.
<i>Salmonella</i> Typhimurium ^{cc}	<i>Salmonella</i> Typhimurium is common worldwide.	<i>Salmonella</i> Typhimurium causes fever, abdominal pain, diarrhea, nausea and sometimes vomiting. Serious complications may occur in a small proportion of cases.	There is no vaccine for <i>Salmonella</i> Typhimurium.	Rehydration is necessary for those made ill. Antibiotic therapy may be indicated for those who are severely symptomatic.	<i>Salmonella</i> Typhimurium could be disseminated by contamination of food or drink.

Disease (Biological Agent)	Ease of Acquisition	Public Health Impact	Prophylaxis	Resistance to Medical Treatment	Ease of Dissemination
Typhoid fever ^{dd} (<i>Salmonella</i> Typhi)	Typhoid fever is found worldwide, with sporadic cases in North America. Most of these cases represent importation from endemic areas.	Generalized systemic enteric fever, headache, malaise, and constipation followed by more severe abdominal symptoms, such as abdominal pain, nausea, vomiting, diarrhea, dehydration may result. The fatality rate with treatment is 1%.	There is an approved oral vaccine against Typhoid fever.	Typhoid fever is successfully treated with antibiotics.	Typhoid fever could be disseminated through food or water contamination.

Source: These data were prepared by the authors from the open literature.

^a Information on glanders is taken from the National Center for Infectious Diseases, "Glanders," Centers for Disease Control and Prevention, found online at [http://www.cdc.gov/ncidod/dbmd/diseaseinfo/glanders_g.htm]; Dahna Batts-Osborne, et al. "CBRNE - Glanders and Melioidosis," eMedicine Knowledge base, found online at [<http://www.emedicine.com/emerg/topic884.htm>]; U.S. Department of Defense, "Field Manual 8-284: Treatment of Biological Warfare Agent Casualties," Washington, D.C., 2000; D. Hank Ellison, *Handbook of Chemical and Biological Warfare Agents*, Boca Raton, FL: CRC Press, 2000; and the Health Canada Material Safety Data Sheet - Infectious Substances for *Burkholderia mallei*.

^b Information on Crimean Congo hemorrhagic fever is taken from the National Center for Infectious Diseases, "Viral Hemorrhagic Fevers," Centers for Disease Control and Prevention, found online at [<http://www.cdc.gov/ncidod/dvrd/spb/mnpages/dispages/vhf.htm>]; the Health Canada Material Safety Data Sheet - Infectious Substances for Crimean Congo hemorrhagic fever; the World Health Organization, "Crimean Congo Hemorrhagic Fever Fact Sheet"; *Handbook of Chemical and Biological Warfare Agents*, op. cit.; and Luciana Borio et al. "Hemorrhagic Fever Viruses as Biological Weapons: Medical and Public Health Management," *Journal of the American Medical Association*, 287 (2002): 2391-2405.

^c Information on pneumonic plague is taken from the Division of Vector-Borne Infectious Diseases, "CDC Plague Home Page," Centers for Disease Control and Prevention, found online at [<http://www.cdc.gov/ncidod/dvbid/plague/index.htm>]; Thomas Inglesby et al. "Plague as a Biological Weapon," *Journal of the American Medical Association* 283(2000):2281-2290; Thomas W. McGovern and Arthur M. Friedlander "Plague," in *Medical Aspects of Chemical and Biological Warfare*, op. cit.; D. Hank Ellison, *Handbook of Chemical and Biological Warfare Agents*, op. cit.; and the Health Canada Material Safety Data Sheet - Infectious Substances for *Yersinia Pestis*.

^d Information on hantavirus is taken from the National Center for Infectious Diseases, "All About Hantaviruses," Centers for Disease Control and Prevention, found online at [<http://www.cdc.gov/ncidod/diseases/hanta/hps/>]; D. Hank Ellison, *Handbook of Chemical and Biological Warfare Agents*, op. cit.; and James N. Mills et al., "Hantavirus Pulmonary Syndrome — United States: Updated Recommendations for Risk Reduction," *Morbidity and Mortality Weekly Report* 51(2002):1-12.

^e Information on dengue hemorrhagic fever is taken from the National Center for Infectious Diseases, "CDC Dengue Fever Home Page," Centers for Disease Control and Prevention found online at [<http://www.cdc.gov/ncidod/dvbid/dengue/index.htm>]; D. Hank Ellison, *Handbook of Chemical and Biological Warfare Agents*, op. cit.; and the Health Canada Material Safety Data Sheet - Infectious Substances for dengue fever.

^f Information on eastern equine encephalitis is taken from the National Center for Infectious Diseases, "Eastern Equine Encephalitis Fact Sheet," Centers for Disease Control and Prevention, found online at [<http://www.cdc.gov/ncidod/dvbid/arbor/eeefact.htm>]; D. Hank Ellison, *Handbook of Chemical and Biological Warfare Agents*, op. cit.; and Mohan Nandalur, and Andrew W. Urban, "Eastern Equine Encephalitis," eMedicine Knowledge base, found online at [<http://www.emedicine.com/med/topic3155.htm>].

- ⁸ Information on Lassa fever is taken from the National Center for Infectious Diseases, "Lassa Fever," Centers for Disease Control and Prevention, found online at [http://www.cdc.gov/ncidod/dvrd/spb/mnpages/dispages/lassa.htm]; D. Hank Ellison, *Handbook of Chemical and Biological Warfare Agents*, *op. cit.*; the World Health Organization, "Lassa Fever," found online at [http://www.who.int/csr/disease/lassafever/en/]; and Luciana Borio *et al.* "Hemorrhagic Fever Viruses as Biological Weapons: Medical and Public Health Management," *op. cit.*
- ⁹ Information on Russian spring-summer encephalitis is taken from the National Center for Infectious Diseases, "Tickborne Encephalitis," Centers for Disease Control and Prevention, found online at [http://www.cdc.gov/travel/diseases/tickenceph.htm]; D. Hank Ellison, *Handbook of Chemical and Biological Warfare Agents*, *op. cit.*; and the Health Canada fact sheet for European Tick Borne Encephalitis, found online at [http://www.hc-sc.gc.ca/pphb-dgspsp/tmp-pmv/travel/tick_e.html].
- ¹⁰ Information on western equine encephalitis is taken from the National Center for Infectious Diseases, "Fact Sheet: Western Equine Encephalitis," Centers for Disease Control and Prevention, found online at [http://www.cdc.gov/ncidod/dvbid/arbor/weefact.htm]; D. Hank Ellison, *Handbook of Chemical and Biological Warfare Agents*, *op. cit.*; and Mohan Nandalur and Andrew W. Urban, "Western Equine Encephalitis," eMedicine Knowledge base, found online at [http://www.emedicine.com/med/topic3156.htm].
- ¹¹ Information on Rift Valley fever is taken from the National Center for Infectious Diseases, "Rift Valley Fever," Centers for Disease Control and Prevention, found online at [http://www.cdc.gov/ncidod/dvrd/spb/mnpages/dispages/rvf.htm]; D. Hank Ellison, *Handbook of Chemical and Biological Warfare Agents*, *op. cit.*; and the World Health Organization, found online at [http://www.who.int/mediacentre/factsheets/fs207/en/].
- ¹² Information on Marburg hemorrhagic fever is taken from the National Center for Infectious Diseases, "Marburg Hemorrhagic Fever," Centers for Disease Control and Prevention, found online at [http://www.cdc.gov/ncidod/dvrd/spb/mnpages/dispages/marburg.htm]; D. Hank Ellison, *Handbook of Chemical and Biological Warfare Agents*, *op. cit.*; and Luciana Borio *et al.*, "Hemorrhagic Fever Viruses as Biological Weapons: Medical and Public Health Management," *op. cit.*
- ¹³ Information on Ebola hemorrhagic fever is taken from the National Center for Infectious Diseases, "Ebola Hemorrhagic Fever," Centers for Disease Control and Prevention, found online at [http://www.cdc.gov/ncidod/dvrd/spb/mnpages/dispages/ebola.htm]; D. Hank Ellison, *Handbook of Chemical and Biological Warfare Agents*, *op. cit.*; and Luciana Borio *et al.*, "Hemorrhagic Fever Viruses as Biological Weapons: Medical and Public Health Management," *op. cit.*
- ¹⁴ Information on melioidosis is taken from the National Center for Infectious Diseases, "Melioidosis," Centers for Disease Control and Prevention, found online at [http://www.cdc.gov/ncidod/dbmd/diseaseinfo/melioidosis_g.htm]; Dahn Batts-Osborne *et al.*, "CBRNE - Glanders and Melioidosis," eMedicine Knowledge base, found online at [http://www.emedicine.com/emerg/topic884.htm]; D. Hank Ellison, *Handbook of Chemical and Biological Warfare Agents*, *op. cit.*; and the Health Canada Material Safety Data Sheet - Infectious Substances for *Burkholderia pseudomallei*, found online at [http://www.hc-sc.gc.ca/pphb-dgspsp/msds-ftss/msds26e.html].
- ¹⁵ Information on yellow fever is taken from the National Center for Infectious Diseases, "Yellow Fever — Disease and Vaccine," Centers for Disease Control and Prevention, found online at [http://www.cdc.gov/ncidod/dvbid/yellowfever/index.htm]; the World Health Organization, "Yellow Fever," found online at [http://www.who.int/health_topics/yellow_fever/en/]; D. Hank Ellison, *Handbook of Chemical and Biological Warfare Agents*, *op. cit.*; and Luciana Borio *et al.* "Hemorrhagic Fever Viruses as Biological Weapons: Medical and Public Health Management," *op. cit.*
- ¹⁶ Information on anthrax is taken from the Centers for Disease Control and Prevention, "Anthrax," found online at [http://www.bt.cdc.gov/agent/anthrax/index.asp]; Frederick R. Sidell, William C. Patrick, III, and Thomas R. Dashiell, *Jane's Chem-Bio Handbook*, *op. cit.*; Arthur M. Friedlander, "Anthrax," in *Medical Aspects of Chemical and Biological Warfare*, *op. cit.*; D. Hank Ellison, *Handbook of Chemical and Biological Warfare Agents*, *op. cit.*; and Thomas V. Inglesby *et al.*, "Anthrax as a Biological Weapon: Medical and Public Health Management," *Journal of the American Medical Association* 281(1999):1735-1745.
- ¹⁷ Information on Q fever is taken from the National Center for Infectious Diseases, "Q Fever," Centers for Disease Control and Prevention, found online at [http://www.cdc.gov/ncidod/dvrd/qfever/]; William R. Byrne, "Q Fever," in *Medical Aspects of Chemical and Biological Warfare* *op. cit.*; the Health Canada Material Safety Data Sheet - Infectious Substances for Q fever, found online at [http://www.hc-sc.gc.ca/pphb-dgspsp/msds-ftss/msds43e.html]; D. Hank Ellison, *Handbook of Chemical and Biological Warfare Agents*, *op. cit.*; and Geoffrey Nochimson, "CBRNE - QFever," eMedicine Knowledge base, found online at [http://www.emedicine.com/emerg/topic492.htm].
- ¹⁸ Information on Machupo hemorrhagic fever is taken from the National Center for Infectious Diseases, "Arenaviruses," Centers for Disease Control and Prevention, found online at [http://www.cdc.gov/ncidod/dvrd/spb/mnpages/dispages/arena.htm]; the Health Canada Material Safety Data Sheet - Infectious Substances for Machupo hemorrhagic fever, found online at [http://www.hc-sc.gc.ca/pphb-dgspsp/msds-ftss/msds89e.html]; D. Hank Ellison, *Handbook of Chemical and Biological Warfare Agents*, *op. cit.*; and Luciana Borio *et al.*, "Hemorrhagic Fever Viruses as Biological Weapons: Medical and Public Health Management," *op. cit.*

- ^r Information on tularemia is taken from the Centers for Disease Control and Prevention, "Tularemia," found online at [http://www.bt.cdc.gov/agent/tularemia/index.asp]; David T. Dennis *et al.*, "Tularemia as a Biological Weapon: Medical and Public Health Management," *Journal of the American Medical Association* 285 (2001):2763-2773; D. Hank Ellison, *Handbook of Chemical and Biological Warfare Agents*, *op. cit.*; and Martin E. Evans and Arthur M. Friedlander, "Tularemia," in *Medical Aspects of Chemical and Biological Warfare*, *op. cit.*
- ^s Information on Junin hemorrhagic fever is taken from the National Center for Infectious Diseases, "Arenaviruses," Centers for Disease Control and Prevention, found online at [http://www.cdc.gov/ncidod/dvrd/spb/mnpages/dispages/arena.htm]; the Health Canada Material Safety Data Sheet - Infectious Substances for Junin hemorrhagic fever, found online at [http://www.hc-sc.gc.ca/pphb-dgspsp/msds-fss/msds89e.html]; D. Hank Ellison, *Handbook of Chemical and Biological Warfare Agents*, *op. cit.*; and Luciana Borio *et al.*, "Hemorrhagic Fever Viruses as Biological Weapons: Medical and Public Health Management," *op. cit.*
- ^t Information on Venezuelan equine encephalitis is taken from the U.S. Department of Defense, "Field Manual 8-284: Treatment of Biological Warfare Agent Casualties," *op. cit.*; D. Hank Ellison, *Handbook of Chemical and Biological Warfare Agents*, *op. cit.*; and Robert Derlet, "CBRNE - Venezuelan Equine Encephalitis," eMedicine Knowledge base, found online at [http://www.emedicine.com/emerg/topic886.htm].
- ^u Information on typhus is taken from the World Health Organization, "Typhus Fever," found online at [http://mednet3.who.int/eml/disease_factsheet.asp?diseaseId=352]; D. Hank Ellison, *Handbook of Chemical and Biological Warfare Agents*, *op. cit.*; and Health Canada Material Safety Data Sheet - Infectious Substances for *Rickettsia prowazekii*, found online at [http://www.hc-sc.gc.ca/pphb-dgspsp/msds-fss/msds128e.html].
- ^v Information on Rocky Mountain spotted fever is taken from the National Center for Infectious Diseases, "Rocky Mountain Spotted Fever," Centers for Disease Control and Prevention, found online at [http://www.cdc.gov/ncidod/dvrd/rmsf/]; D. Hank Ellison, *Handbook of Chemical and Biological Warfare Agents*, *op. cit.*; and the Health Canada Material Safety Data Sheet - Infectious Substances for *Rickettsia rickettsii*, found online at [http://www.hc-sc.gc.ca/pphb-dgspsp/msds-fss/msds129e.html].
- ^w Information on *Escherichia coli* O157:H7 is taken from the Center for Food Safety and Applied Nutrition, "Escherichia coli O157:H7," *Foodborne Pathogenic Microorganisms and Natural Toxins Handbook*, Washington, D.C.: U.S. Food and Drug Administration, 1992, found online at [http://vm.cfsan.fda.gov/~mow/chap15.html]; the National Center for Infectious Diseases, "*Escherichia coli* O157:H7," Centers for Disease Control and Prevention, found online at [http://www.cdc.gov/ncidod/dbmd/diseaseinfo/escherichiacoli_g.htm]; the Health Canada Material Safety Data Sheet - Infectious Substances for *Escherichia coli* O157:H7, found online at [http://www.hc-sc.gc.ca/pphb-dgspsp/msds-fss/msds63e.html]; D. Hank Ellison, *Handbook of Chemical and Biological Warfare Agents*, *op. cit.*; and the World Health Organization, "*Escherichia coli* Infections," found online at [http://www.who.int/health_topics/escherichia_coli_infections/en/].
- ^x Information on smallpox is taken from the Centers for Disease Control and Prevention "Smallpox", found online at [http://www.bt.cdc.gov/agent/smallpox/index.asp]; D. Hank Ellison, *Handbook of Chemical and Biological Warfare Agents*, *op. cit.*; David J. McClain, "Smallpox," in *Medical Aspects of Chemical and Biological Warfare*, *op. cit.*; and Donald A. Henderson *et al.*, "Smallpox as a Biological Weapon: Medical and Public Health Management," *Journal of the American Medical Association* 281 (1999):2127-2137.
- ^y Information on monkeypox is taken from National Center for Infectious Diseases, "Monkeypox," Centers for Disease Control and Prevention, found online at [http://www.cdc.gov/ncidod/monkeypox/index.htm] and Yvan J.F. Hutin *et al.*, "Outbreak of Human Monkeypox, Democratic Republic of Congo, 1996 to 1997," *Emerging Infectious Diseases* 17 (2001):434-438.
- ^z Information on brucellosis is taken from the National Center for Infectious Diseases, "Brucellosis," Centers for Disease Control and Prevention, found online at [http://www.cdc.gov/ncidod/dbmd/diseaseinfo/brucellosis_g.htm]; D. Hank Ellison, *Handbook of Chemical and Biological Warfare Agents*, *op. cit.*; and David L. Hoover and Arthur M. Friedlander, "Brucellosis," in *Medical Aspects of Chemical and Biological Warfare*, *op. cit.*
- ^{aa} Information on *Shigella dysenteriae* is taken from the National Center for Infectious Diseases, "Shigellosis," Centers for Disease Control and Prevention, found online at [http://www.cdc.gov/ncidod/dbmd/diseaseinfo/shigellosis_g.htm]; Center for Food Safety and Applied Nutrition, "*Shigella* Spp.," *Foodborne Pathogenic Microorganisms and Natural Toxins Handbook*, *op. cit.*, found online at [http://vm.cfsan.fda.gov/~mow/chap19.htm]; D. Hank Ellison, *Handbook of Chemical and Biological Warfare Agents*, *op. cit.*; and the Health Canada Material Safety Data Sheet - Infectious Substances for *Shigella* spp., found online at [http://www.hc-sc.gc.ca/pphb-dgspsp/msds-fss/msds139e.html].
- ^{bb} Information on cholera is taken from the National Center for Infectious Diseases, "Cholera," Centers for Disease Control and Prevention, found online at [http://www.cdc.gov/ncidod/dbmd/diseaseinfo/cholera_g.htm]; the Health Canada Material Safety Data Sheet - Infectious Substances for *Vibrio cholerae*, found online at [http://www.hc-sc.gc.ca/pphb-dgspsp/msds-fss/msds164e.html]; D. Hank Ellison, *Handbook of Chemical and Biological Warfare Agents*, *op. cit.*; and the World Health Organization, "Cholera and Epidemic-prone Diarrhoeal Diseases," found online at [http://www.who.int/csr/disease/cholera/en/].

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^{cc} Information on *Salmonella* Typhimurium is taken from the National Center for Infectious Diseases, “Salmonellosis,” Centers for Disease Control and Prevention, found online at [http://www.cdc.gov/ncidod/dbmd/diseaseinfo/salmonellosis_g.htm] and Center for Food Safety and Applied Nutrition, “*Salmonella* Spp.,” *Foodborne Pathogenic Microorganisms and Natural Toxins Handbook*, *op. cit.*

^{dd} Information on typhoid fever is taken from the National Center for Infectious Diseases, “Typhoid Fever,” Centers for Disease Control and Prevention, found online at [http://www.cdc.gov/ncidod/dbmd/diseaseinfo/typhoidfever_g.htm]; D. Hank Ellison, *Handbook of Chemical and Biological Warfare Agents*, *op. cit.*; and the Health Canada Material Safety Data Sheet - Infectious Substances for typhoid fever, found online at [<http://www.hc-sc.gc.ca/pphb-dgspsp/msds-floss/msds134e.html>], and Center for Food Safety and Applied Nutrition, “*Salmonella* Spp.,” *Foodborne Pathogenic Microorganisms and Natural Toxins Handbook*, *op. cit.*

Appendix D

Table 6. Comparison of toxin agent characteristics

Toxins	Ease of Acquisition	Public Health Impact	Prophylaxis	Resistance to Medical Treatment	Ease of Dissemination
Abrin ^a	Abrin can be isolated from seeds of <i>Abrus precatorius</i> , the rosary pea plant. This plant is commonly found in many parts of the world, including the United States.	Aerosol abrin exposure causes weakness, fever, cough, and pulmonary edema. Ingestion of abrin causes abdominal pains, vomiting, diarrhea, and death. The lethal dosage which will kill 50% of those exposed (LD ₅₀) for aerosol exposure is 0.04 micrograms per kilogram (mcg/kg). (see Table Note).	There is currently no vaccine or prophylactic antitoxin available for human use.	Other than supportive care, there is no specific treatment for abrin exposure	Abrin could be disseminated either by aerosol or through contamination of food or water.
Shigatoxin ^b	Shigatoxin is a potent toxin produced by members of the <i>Shigella</i> bacteria family. This bacteria is ubiquitous.	Ingestion of shigatoxin can cause severe intestinal damage and kidney failure. Aerosol exposure is expected to cause pneumonic symptoms. The LD ₅₀ for aerosol exposure is 0.002 mcg/kg.	There is currently no vaccine or prophylactic antitoxin available for human use.	Other than supportive care, there is no specific treatment for shigatoxin exposure.	Shigatoxin could be disseminated either by aerosol or through contamination of food or water.
Ricin ^c	Ricin can be isolated from castor beans and is a by product of castor oil production. Approximately 1 million tons of beans are processed annually worldwide.	Aerosol ricin exposure causes weakness, fever, cough, and pulmonary edema within 18-24 hours and severe respiratory distress and death within 36-72 hours. Ingestion of ricin causes abdominal pains, vomiting, diarrhea, and death. The LD ₅₀ for aerosol exposure is 3 mcg/kg.	There is currently no vaccine or prophylactic antitoxin available for human use. A vaccine is in IND drug testing.	Other than supportive care, there is no specific treatment for ricin exposure	Ricin could be disseminated either by aerosol or through contamination of food or water.

Toxins	Ease of Acquisition	Public Health Impact	Prophylaxis	Resistance to Medical Treatment	Ease of Dissemination
<i>Clostridium perfringens</i> epsilon toxin ^d	This toxin is one of several toxins produced by <i>Clostridium perfringens</i> bacteria. These are widely distributed in nature and frequently occur in the intestines of humans and many animals.	Ingestion of <i>Clostridium perfringens</i> epsilon toxin causes intense abdominal cramps and diarrhea. Aerosol exposure to <i>Clostridium perfringens</i> epsilon toxin would cause pneumonia-like symptoms. The LD ₅₀ for aerosol exposure is 0.1 - 5.0 mcg/kg.	There is currently no vaccine or prophylactic antitoxin available for human use. Antitoxins are in animal studies.	Other than supportive care, there is no specific treatment for <i>Clostridium perfringens</i> epsilon toxin.	<i>Clostridium perfringens</i> epsilon toxin could be disseminated either by aerosol or through contamination of food or water.
<i>Staphylococcus aureus</i> enterotoxin B ^e	This toxin is one of several toxins made by many strains of the bacterium <i>Staphylococcus aureus</i> . This bacteria is ubiquitous.	Aerosol exposure to <i>Staphylococcus aureus</i> enterotoxin B causes fever, chills, headache, muscle pain, and cough. The fever may last 2 to five days, and the cough may persist for up to four weeks. Victims who ingest the toxin suffer nausea, vomiting, and diarrhea. Higher exposure can lead to septic shock and death. The LD ₅₀ for aerosol exposure is 27 mcg/kg.	There is currently no vaccine or prophylactic antitoxin available for human use. Antitoxins are in animal trials.	Other than supportive care, there is no specific treatment for <i>Staphylococcus aureus</i> enterotoxin B exposure.	<i>Staphylococcus aureus</i> enterotoxin B could be disseminated either by aerosol or through contamination of food or water.

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Toxins	Ease of Acquisition	Public Health Impact	Prophylaxis	Resistance to Medical Treatment	Ease of Dissemination
Trichothecene mycotoxins ^f	The trichothecene mycotoxins are produced by molds. These molds are found in nature, but only produce these toxins under specific conditions.	Contact exposure to the mycotoxins causes burning, tender and reddened skin, swelling, and blistering, which progresses to tissue death. In lethal cases, sloughing of large skin areas occurs. Aerosol exposure to the mycotoxins results in nasal itching, pain, sneezing, bloody and runny nose, difficulty breathing, and cough. Ingestion of the mycotoxins causes loss of appetite, nausea and vomiting, abdominal cramping, and bloody diarrhea. The LD ₅₀ for aerosol exposure 1,210 mcg/kg.	There is currently no vaccine or prophylactic antitoxin available for human use.	Other than supportive care, there is no specific treatment for trichothecene mycotoxin exposure.	Trichothecene mycotoxins could be disseminated either by aerosol or through contamination of food or water.
Aflatoxins ^g	Aflatoxin is a naturally occurring toxin produced by some molds. These molds are common in nature, and aflatoxin is produced when these molds are grown under stressful conditions. Some foods in the U.S. are regularly tested for the presence of aflatoxins.	Exposure to aflatoxins can cause hemorrhage, liver damage, edema, alteration in digestion, absorption and/or metabolism of nutrients, and possibly death. The LD ₅₀ for aflatoxin is 10 mg/kg.	There is currently no vaccine or prophylactic antitoxin available for human use.	There is no specific treatment for aflatoxin exposure.	Aflatoxin could be disseminated either by aerosol or through contamination of food or water.

Toxins	Ease of Acquisition	Public Health Impact	Prophylaxis	Resistance to Medical Treatment	Ease of Dissemination
<i>Clostridium botulinum</i> toxins ^b	There are seven types of toxin produced by <i>Clostridium botulinum</i> bacteria. These bacteria are ubiquitous in soil and can often be found in poorly preserved, canned food.	Ingestion of botulinum toxin causes difficulty speaking, seeing and/or swallowing, leading to increasing paralysis that may include respiratory paralysis. Recovery from paralysis can take from weeks to months. Inhalation of botulinum toxin causes more rapid onset of symptoms. The LD ₅₀ for aerosol exposure is 0.001 mcg/kg.	There is currently an unlicensed botulinum toxoid vaccine available for human use.	Exposure to botulinum toxin can be treated with antitoxin. This treatment stops further damage, but does not reverse current paralysis. Mechanical breathing assistance and supportive care are required in acute cases.	<i>Clostridium botulinum</i> toxins could be disseminated either by aerosol or through contamination of food or water.
Saxitoxin ⁱ	Saxitoxin is a neurotoxin produced by marine dinoflagellates. These microorganisms live in shellfish.	Ingestion of saxitoxin is commonly known as paralytic shellfish poisoning. Saxitoxin causes numbness of the lips, tongue and fingertips, followed by neck and extremities, and a lack of coordination. Respiratory distress and paralysis are the terminal stages and can occur within 2-12 hours. Death results from respiratory paralysis. Aerosol exposure to saxitoxin compresses the onset of symptoms and death may occur in minutes. The LD ₅₀ for aerosol exposure is 0.002 mcg/kg.	There is currently no vaccine or prophylactic antitoxin available for human use.	Other than supportive care, mechanical ventilation to relieve respiratory distress is the only treatment for saxitoxin exposure.	Saxitoxin could be disseminated either by aerosol or through contamination of food or water.

Toxins	Ease of Acquisition	Public Health Impact	Prophylaxis	Resistance to Medical Treatment	Ease of Dissemination
Tetrodotoxin ^j	Tetrodotoxin is most commonly found in the pufferfish.	Tetrodotoxin ingestion causes a slight numbness of the lips and tongue, followed by increasing paralysis. Death usually occurs within 4 to 6 hours. Aerosol exposure is expected to cause more rapid onset of symptoms. The LD ₅₀ for aerosol exposure is 8.0 mcg/kg.	There is currently no vaccine or prophylactic antitoxin available for human use. Antitoxins are in animal studies.	Other than supportive care, mechanical ventilation to relieve respiratory distress is the only treatment for tetrodotoxin exposure.	Tetrodotoxin could be disseminated either by aerosol or through contamination of food or water.

Source: These data were prepared by the authors from the open literature.

Note: The LD₅₀ is the dosage of agent per unit body weight required to kill 50% of those exposed. It is expressed here in micrograms (mcg) per kilogram (kg). A microgram weighs approximately as much as the ink used to print a single character on this sheet of paper. A 155 lb. person weighs approximately 70 kilograms.

^a Information on abrin is taken from the Ethnobotany Material Safety Data Sheet for precatory pea, found online at

[<http://www.smm.org/research/Collections/PrecPea.pdf>]; Agriculture and Agri-Food Canada, "Notes on poisoning: *Abrus precatorius*," found online at [http://sis.agr.gc.ca/ppls/pp/ppack.info?p_psn=139&p_type=all&p_sci=sci&p_x=px]; and David R. Franz, "Defense Against Toxin Weapons," in *Medical Aspects of Chemical and Biological Warfare*, *op. cit.*

^b Information on shigatoxin is taken from the National Center for Infectious Diseases, "Shigellosis," Centers for Disease Control and Prevention *op. cit.*; Center for Food Safety and Applied Nutrition, "*Shigella* Spp.," *Foodborne Pathogenic Microorganisms and Natural Toxins Handbook*, *op. cit.*; and David R. Franz, "Defense Against Toxin Weapons," in *Medical Aspects of Chemical and Biological Warfare*, *op. cit.*

^c Information on ricin is taken from U.S. Department of Defense, "Field Manual 8-284: Treatment of Biological Warfare Agent Casualties," *op. cit.*; "CBRNE - Ricin," by Ferdinando L. Mirarchi and Michael Allswede, eMedicine Knowledge base, found online at [<http://www.emedicine.com/emerg/topic889.htm>]; and David R. Franz, and Nancy K. Jaax, "Ricin Toxin," *Medical Aspects of Chemical and Biological Warfare* *op. cit.* For more information on ricin see CRS Report RS21383 *Ricin: Technical Background and Potential Role in Terrorism* by Dana Shea and Frank Gotttron.

^d Information on *Clostridium perfringens* epsilon toxin is taken from U.S. Department of Defense, "Field Manual 8-284: Treatment of Biological Warfare Agent Casualties," *op. cit.*; David R. Franz, "Defense Against Toxin Weapons," in *Medical Aspects of Chemical and Biological Warfare*, *op. cit.*; Center for Food Safety and Applied Nutrition, "*Clostridium perfringens*," *Foodborne Pathogenic Microorganisms and Natural Toxins Handbook*, *op. cit.*

^e Information on *Staphylococcus aureus* enterotoxin B is taken from U.S. Department of Defense, "Field Manual 8-284: Treatment of Biological Warfare Agent Casualties," *op. cit.*; the Federation of American Scientists Special Weapons Primer, found online at [<http://www.fas.org/nuke/intro/bw/agent.htm>]; David R. Franz, "Defense Against Toxin Weapons," in *Medical Aspects of Chemical and Biological Warfare*, *op. cit.*; Robert G. Ulrich *et al.*, "Staphylococcal Enterotoxin B and Related Pyrogenic Toxins," in *Medical Aspects of Chemical and Biological Warfare*, *op. cit.*; and Joanne Williams, "CBRNE - Staphylococcal Enterotoxin B," eMedicine Knowledge base, found online at [<http://www.emedicine.com/emerg/topic888.htm>].

^f Information on Trichothecene mycotoxins is taken from Robert W. Wannemacher, Jr. and Stanley L. Wiener, "Trichothecene Mycotoxins," in *Medical Aspects of Chemical and Biological Warfare*, *op. cit.*; and David R. Franz, "Defense Against Toxin Weapons," in *Medical Aspects of Chemical and Biological Warfare*, *op. cit.*

- ⁸ Information on aflatoxin is taken from the Center for Food Safety and Applied Nutrition, "Aflatoxins," *Foodborne Pathogenic Microorganisms and Natural Toxins Handbook*, *op. cit.*; and from the Office of the Special Assistant to the Deputy Secretary of Defense for Gulf War Illnesses, Medical Readiness, and Military Deployments, "Close-out Report: Biological Warfare Investigation," U.S. Department of Defense, February 13, 2001, found on line at [http://www.gulflink.osd.mil/bw_ii/index.html].
- ⁹ Information on *Clostridium botulinum* toxins is taken from the Center for Food Safety and Applied Nutrition, "Clostridium botulinum," *Foodborne Pathogenic Microorganisms and Natural Toxins Handbook*, *op. cit.*; National Center for Infectious Diseases, "Botulism," Centers for Disease Control and Prevention Centers for Disease Control and Prevention, found online at [http://www.cdc.gov/ncidod/dbmd/diseaseinfo/botulism_g.htm]; Stephen S. Arnon *et al.*, "Botulinum Toxin as a Biological Weapon: Medical and Public Health Management," *Journal of the American Medical Association* 285 (2001):1059-1070; U.S. Department of Defense, "Field Manual 8-284: Treatment of Biological Warfare Agent Casualties," *op. cit.*; John L. Middlebrook and David R. Franz, "Botulinum Toxins," in *Medical Aspects of Chemical and Biological Warfare*, *op. cit.*
- ¹⁰ "Defense Against Toxin Weapons," in *Medical Aspects of Chemical and Biological Warfare*, *op. cit.*; David R. Franz, "Defense Against Toxin Weapons," in *Medical Aspects of Chemical and Biological Warfare*, *op. cit.*; and the Federation of American Scientists Special Weapons Primer, found online at [<http://www.fas.org/nuke/intro/bw/agent.htm>].
- ¹¹ Information on tetrodotoxin is taken from the Center for Food Safety and Applied Nutrition, "Tetrodotoxin," *Foodborne Pathogenic Microorganisms and Natural Toxins Handbook*, *op. cit.*; Theodore Benzer, "Toxicity, Tetrodotoxin," eMedicine Knowledge base, found online at [<http://www.emedicine.com/emerg/topic576.htm>]; and David R. Franz, "Defense Against Toxin Weapons," in *Medical Aspects of Chemical and Biological Warfare*, *op. cit.*

Exhibit B



Sarin attack remembered in Tokyo

Railway staff, survivors and the Japanese prime minister have paid their respects at a shrine in Tokyo, 10 years after the city's subway gas attack.

In a Sunday morning ceremony officials prayed and left flowers for those killed when sarin nerve gas was released on underground trains.

Twelve people died and 5,000 were left with damaged health after the attack by the Aum Shinrikyo cult.

The re-named sect offered a "heartfelt apology" for the act.

Thirteen members of the cult have been sentenced to death over the attack and other crimes.

They include the founder of the "Supreme Truth" movement Shoko Asahara.

None of the death sentences have yet been carried out.

Still suffering

On March 20, 1995, five sect members burst plastic bags filled with the poisonous gas during the morning rush hour.

The cult believed the world was about to be plunged into an apocalyptic war.

As well as the dozen people killed, thousands were injured. Many of them still suffer from headaches, breathing troubles and dizziness.

At 0800 on Sunday, (2300 GMT Saturday), subway staff led the commemorations at a temporary shrine.

"Even now I remember it so vividly. Frankly, I'd rather not talk about it," said Tatsuhide Nojiri, who was chief of one of the railway stations attacked.

Later in the day Prime Minister Junichiro Koizumi and government colleagues prayed before the altar.

Japanese security services say Aum has far fewer members than the 40,000 followers it had in 1995, but still exists under a new name, Aleph.

The group has promised to pay millions of dollars in damages to victims, but has come up with less than half of what it pledged.

Story from BBC NEWS:
<http://news.bbc.co.uk/go/pr/fr/-/2/hi/asia-pacific/4365417.stm>

Published: 2005/03/20 08:16:59 GMT

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Exhibit C

CENTRAL INTELLIGENCE AGENCY



DIRECTORATE OF INTELLIGENCE

Terrorist CBRN:

Materials and Effects (U)



May 2003

CTC 2003-40058

Terrorist CBRN: Materials and Effects

Background

Al-Qa'ida and associated extremist groups have a wide variety of potential agents and delivery means to choose from for chemical, biological, radiological, or nuclear (CBRN) attacks. Al-Qa'ida's end goal is the use of CBRN to cause mass casualties; however, most attacks by the group—and especially by associated extremists—probably will be small scale, incorporating relatively crude delivery means and easily produced or obtained chemicals, toxins, or radiological substances. The success of any al-Qa'ida attack and the number of ensuing casualties would depend on many factors, including the technical expertise of those involved, but most scenarios could cause panic and disruption.

- Several groups of mujahidin associated with al-Qa'ida have attempted to carry out "poison plot" attacks in Europe with easily produced chemicals and toxins best suited to assassination and small-scale scenarios. These agents could cause hundreds of casualties and widespread panic if used in multiple simultaneous attacks.
- Al-Qa'ida is interested in radiological dispersal devices (RDDs) or "dirty bombs." Construction of an RDD is well within its capabilities as radiological materials are relatively easy to acquire from industrial or medical sources. Usama Bin Ladin's operatives may try to launch conventional attacks against the nuclear industrial infrastructure of the United States in a bid to cause contamination, disruption, and terror.
- A document recovered from an al-Qa'ida facility in Afghanistan contained a sketch of a crude nuclear device.
- Spray devices disseminating biological warfare (BW) agents have the highest potential impact. Both 11 September attack leader Mohammad Atta and Zacharias Moussaoui expressed interest in crop dusters, raising our concern that al-Qa'ida has considered using aircraft to disseminate BW agents.
- Analysis of an al-Qa'ida document recovered in Afghanistan in summer 2002 indicates the group has

crude procedures for making mustard agent, sarin, and VX.

This pamphlet contains a summary of typical agents and CBRN devices available to al-Qa'ida and other terrorist groups. It is not intended to be a summary of the overall threat from al-Qa'ida's CBRN program.

Chemical Agents

Terrorists have considered a wide range of toxic chemicals for attacks. Typical plots focus on poisoning foods or spreading the agent on surfaces to poison via skin contact, but some also include broader dissemination techniques.

Cyanides

Terrorists have considered using a number of toxic cyanide compounds.

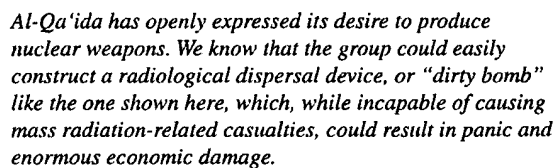
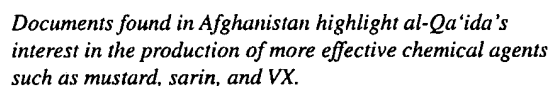
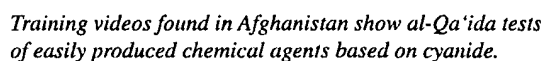
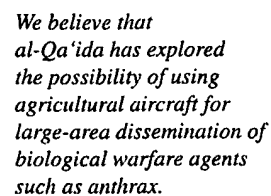
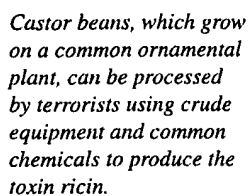
Sodium or potassium cyanides are white-to-pale yellow salts that can be easily used to poison food or drinks. Cyanide salts can be disseminated as a contact poison when mixed with chemicals that enhance skin penetration, but may be detected since most people will notice if they touch wet or greasy surfaces contaminated with the mixture.


Hydrogen cyanide (HCN) and cyanogen chloride (CICN) are colorless-to-pale yellow liquids that will turn into a gas near room temperature. HCN has a characteristic odor of bitter almonds, and CICN has an acrid choking odor and causes burning pain in the victim's eyes. These signs may provide enough warning to enable evacuation or ventilation of the attack site before the agent reaches a lethal concentration.

- Both HCN and CICN need to be released at a high concentration—only practical in an enclosed area—to be effective, therefore, leaving the area or ventilating will significantly reduce the agent's lethality.

Exposure to cyanide may produce nausea, vomiting, palpitations, confusion, hyperventilation, anxiety, and vertigo that may progress to agitation, stupor, coma,

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and death. At high doses, cyanides cause immediate collapse. Medical treatments are available, but they need to be used immediately for severely exposed victims.

Mustard Agent

Mustard is a blister agent that poses a contact and vapor hazard. Its color ranges from clear to dark brown depending on purity, and it has a characteristic garlicklike odor. Mustard is a viscous liquid at room temperature.

- Mustard is not commercially available, but its synthesis does not require significant expertise if a step-by-step procedure with diagrams is available.

Initial skin contact with mustard causes mild skin irritation, which develops into more severe yellow fluid-filled blisters. Inhalation of mustard damages the lungs, causes difficulty breathing, and death by suffocation in severe cases due to water in the lungs. For both skin contact and inhalation, symptoms appear within six to 24 hours. There are only limited medical treatments available for victims of mustard-agent poisoning.

Nerve Agents

Sarin, tabun, and VX are highly toxic military agents that disrupt a victim's nervous system by blocking the transmission of nerve signals.

- These agents are not commercially available, and their synthesis requires significant chemical expertise.

Exposure to nerve agents causes pinpoint pupils, salivation, and convulsions that can lead to death. Medical treatments are available, but they need to be used immediately for severely exposed victims.

Toxic Industrial Chemicals

There are a wide range of toxic industrial chemicals that—while not as toxic as cyanide, mustard, or nerve agents—can be used in much larger quantities to compensate for their lower toxicity.

Chlorine and phosgene are industrial chemicals that are transported in multiton shipments by road and rail. Rupturing the container can easily disseminate these gases. The effects of chlorine and phosgene are similar to those of mustard agent.

Organophosphate pesticides such as parathion are in the same chemical class as nerve agents. Although these pesticides are much less toxic, their effects and medical treatments are the same as for military-grade nerve agents.

Biological Agents

Anthrax

Bacillus anthracis, the bacterium that causes anthrax, is capable of causing mass casualties. Symptoms usually appear within one to six days after exposure and include fever, malaise, fatigue, and shortness of breath. The disease is usually fatal unless antibiotic treatment is started within hours of inhaling anthrax spores; however, it is not contagious. Few people are vaccinated against anthrax.

- Anthrax can be disseminated in an aerosol or used to contaminate food and water.
- Cutaneous anthrax can be caused by skin contact with *B. anthracis*. This form of the disease, which is easily treated with antibiotics, is rarely fatal.

Botulinum toxin

Botulinum toxin is produced by the bacterium *Clostridium botulinum*, which occurs naturally in the soil. Crude but viable methods to produce small quantities of this lethal toxin have been found in terrorist training manuals.

- Symptoms usually occur 24 to 36 hours after exposure, but onset of illness may take several days if the toxin is present in low doses. They include vomiting, abdominal pain, muscular weakness, and visual disturbance.
- Botulinum toxin would be effective in small-scale poisonings or aerosol attacks in enclosed spaces, such as movie theaters. The toxin molecule is likely too large to penetrate intact skin.

Ricin

Ricin is a plant toxin that is 30 times more potent than the nerve agent VX by weight and is readily obtainable by extraction from common castor beans.

There is no treatment for ricin poisoning after it has entered the bloodstream. Victims start to show symptoms within hours to days after exposure, depending on the dosage and route of administration.

- Terrorists have looked at delivering ricin in foods and as a contact poison, although we have no scientific data to indicate that ricin can penetrate intact skin.
- Ricin will remain stable in foods as long as they are not heated, and it will have few indicators because it does not have a strong taste and is off-white in color.

Radiological and Nuclear Devices

Radiological Dispersal Devices (RDD)

An RDD is a conventional bomb not a yield-producing nuclear device. RDDs are designed to disperse radioactive material to cause destruction, contamination, and injury from the radiation produced by the material. An RDD can be almost any size, defined only by the amount of radioactive material and explosives.

- A passive RDD is a system in which unshielded radioactive material is dispersed or placed manually at the target.
- An explosive RDD—often called a “dirty bomb”—is any system that uses the explosive force of detonation to disperse radioactive material. A simple explosive RDD consisting of a lead-shielded container—commonly called a “pig”—and a kilogram of explosive attached could easily fit into a backpack.
- An atmospheric RDD is any system in which radioactive material is converted into a form that is easily transported by air currents.

Use of an RDD by terrorists could result in health, environmental, and economic effects as well as political and social effects. It will cause fear, injury, and possibly lead to levels of contamination requiring costly and time-consuming cleanup efforts.

A variety of radioactive materials are commonly available and could be used in an RDD, including Cesium-137, Strontium-90, and Cobalt-60. Hospitals, universities, factories, construction companies, and laboratories are possible sources for these radioactive materials.

Improvised Nuclear Device (IND)

An IND is intended to cause a yield-producing nuclear explosion. An IND could consist of diverted nuclear weapon components, a modified nuclear weapon, or indigenous-designed device.

- INDs can be categorized into two types: implosion and gun assembled. Unlike RDDs that can be made with almost any radioactive material, INDs require fissile material—highly enriched uranium or plutonium—to produce nuclear yield.

Online Resources

More detailed information on the medical aspects of chemical, biological, and nuclear weapons threats can be found at the following Internet sites:

The Medical NBC Information server:

www.nbc-med.org and <http://www.nbc-med.org>

Medical Research and Material Command:

mrmc-www.army.mil

Medical Research Institute of Chemical Defense:

chemdef.apgea.army.mil

Medical Research Institute of Infectious Diseases:

www.usamriid.army.mil

National Institute for Occupational Safety and Health: www.cdc.gov/niosh/topics/chemical-safety/default.html

US Department of Homeland Security:

www.ready.gov

Central Intelligence Agency:

CBR Incident Handbook www.cia.gov/CIA/Publications/cbr-handbook/cbrbook.html

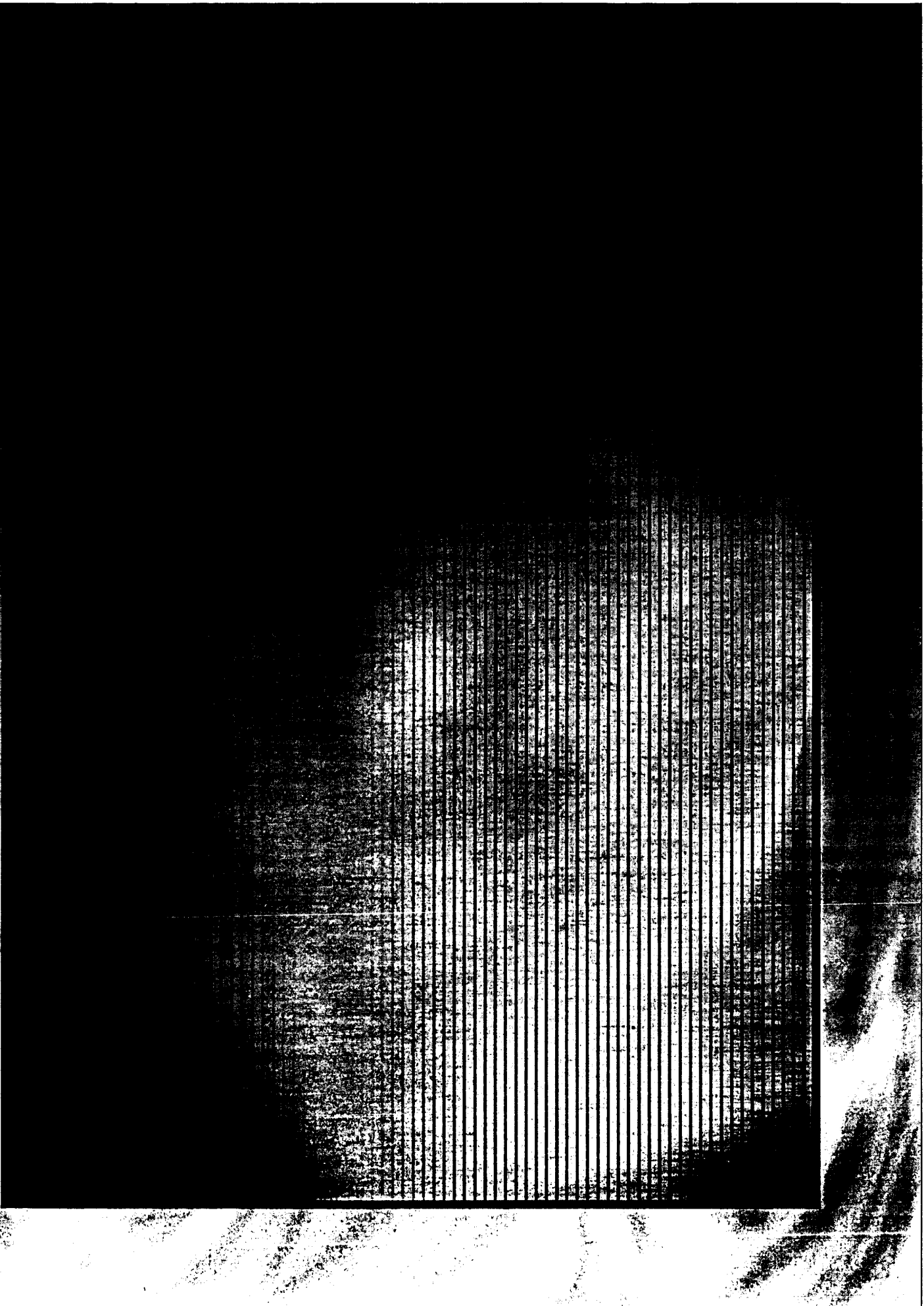


Exhibit D



TOXIC SYNDROME DESCRIPTION

Nerve Agents and Organophosphate Pesticides

The purpose of this document is to enable health care workers and public health officials to recognize an unknown or suspected exposure to a nerve agent or an organophosphate (OP) pesticide. Nerve agents are chemical warfare agents that have the same mechanism of action as OP pesticides. They are potent inhibitors of acetylcholinesterase. Inhibition of acetylcholinesterase leads to an accumulation of acetylcholine in the central and peripheral nervous system. Excess acetylcholine produces a predictable cholinergic syndrome consisting of copious respiratory and oral secretions, diarrhea and vomiting, sweating, altered mental status, autonomic instability, and generalized weakness that can progress to paralysis and respiratory arrest.

The amount and route of exposure to the nerve agent or OP pesticide, the type of agent or pesticide, and the premorbid condition of the exposed person will contribute to the time of onset and the severity of illness. For example, inhalation of a nerve agent or an OP pesticide leads to a quicker onset of poisoning with more severe symptoms compared with dermal exposure, given the same amount of agent.

Signs and symptoms

The following is a more comprehensive list of signs and symptoms that may be encountered in a person exposed to a nerve agent or OP pesticide. Signs and symptoms are not listed in order of presentation or specificity. Also, partial presentations (an absence of some of the following signs/symptoms) do not necessarily imply less severe disease.

Central nervous system signs and symptoms

- Miosis (unilateral or bilateral)
- Headache
- Restlessness
- Convulsions
- Loss of consciousness
- Coma

Respiratory signs and symptoms

- Rhinorrhea (profuse watery runny nose)
- Bronchorrhea (excessive bronchial secretions)
- Wheezing
- Dyspnea (shortness of breath)
- Chest tightness
- Hyperpnea (increased respiratory rate/depth)—early
- Bradypnea (decreased respiratory rate)—late

Toxic Syndrome Description for Nerve Agents and Organophosphate Pesticides

(continued from previous page)

Cardiovascular signs

- Tachycardia (increased heart rate)—early
- Hypertension (high blood pressure)—early
- Bradycardia (decreased heart rate)—late
- Hypotension (low blood pressure)—late
- Dysrhythmias (prolonged QT on EKG, ventricular tachycardia)

Gastrointestinal signs and symptoms

- Abdominal pain
- Nausea and vomiting
- Diarrhea
- Urinary incontinence, frequency

Musculoskeletal signs and symptoms

- Weakness (may progress to paralysis)
- Fasciculations (local or generalized)

Skin and mucous membrane signs and symptoms

- Profuse sweating (local or generalized)
- Lacrimation (tear formation)
- Conjunctival injection

Laboratory finding suggestive of nerve agent poisoning

- Decreased plasma or red blood cell (RBC) cholinesterase activity

Limitations

- Wide normal range for enzyme activity makes interpretation difficult without a baseline measurement.
- Cholinesterase activity correlates poorly with severity of local effects after vapor exposures.
- Plasma or RBC cholinesterase may be disproportionately inhibited depending on the particular nerve agent, amount of exposure and time interval since exposure.

Interpreting cholinesterase activity

- Plasma cholinesterase
 - usually declines faster than RBC cholinesterase;
 - is easier to assay than RBC cholinesterase;
 - regenerates faster than RBC cholinesterase;
 - may have a day-to-day variation in enzyme activity as high as 20%;
 - is less specific than RBC cholinesterase; and
 - can show false depression from liver disease, malnutrition, pregnancy, genetic deficiency, or drugs (e.g., codeine, morphine, cocaine, succinylcholine).
- Red blood cell cholinesterase
 - is a better reflection of CNS cholinesterase activity;
 - is more specific test than plasma cholinesterase;
 - may have a day-to-day variation in enzyme activity as high as 10%; and

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Toxic Syndrome Description for Nerve Agents and Organophosphate Pesticides (continued from previous page)

- can show false depression from antimalarial therapy or pernicious anemia.

Differential diagnosis

- Carbamate insecticides
- Medicinal carbamates (eg, pyridostigmine, neostigmine, physostigmine)
- Cholinomimetic compounds (eg, pilocarpine, methacholine, bethanechol)
- Nicotine alkaloids (eg, nicotine, coniine)
- Muscarine-containing mushrooms
- Neuromuscular blocking drugs (eg, atracurim, vecuronium)

Note: The actual clinical manifestations of an exposure to a nerve agent or an organophosphate pesticide may be more variable than the syndrome described in this document.

This toxic syndrome description is based on CDC's best current information.
It may be updated as new information becomes available.

For more information, visit www.bt.cdc.gov/chemical, or call CDC at
800-CDC-INFO (English and Spanish) or 888-232-6348 (TTY).

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Exhibit E



Push for anti-nerve agent drug

By Paul Rincon
BBC News Online science staff

Molecules that destroy deadly nerve agents could provide the basis of a new type of civilian drug to protect people against a terrorist attack.

The US army is testing the enzymes - called paraoxonases - to see if they could be used to protect troops from exposure during battle.

But Israeli researchers working in the field say any new drug could also have a role in the civil defence setting.

However, the new technology is likely to take some years to develop and test.

The paraoxonases might also have applications as sprays to decontaminate areas and groups of people exposed to nerve agents.

Paraoxonases are a particularly attractive choice as the basis for developing pre-treatment drugs, or prophylactics, because they completely break down organophosphorus nerve agents like sarin, the agent used in the Tokyo underground attack in March 1995.

Ongoing protection

Neither of the current prophylactics in use by the military, or in development, work in this way.

Another anti-nerve agent enzyme known as butyrylcholinesterase works by binding to organophosphates, preventing them from doing any harm. But as the enzymes bind to organophosphorus molecules they are used up.

When people are given things to self-administer they will often overdose in anticipation of an attack
Dr Sally Lievesley

Paraoxonases could break down organophosphates and regenerate, continuing to work even after multiple exposures to nerve agents - so long as the enzymes are present in the bloodstream.

Dr David Lenz, of the US Army Medical Research Institute of Chemical Defense, in Maryland, US, told BBC News Online that the army was to begin testing the paraoxonases to see if they could be turned into prophylactics to be administered to American troops operating in zones at risk of a chemical attack.

"We are trying to develop proteins of human origin that we could administer to people as drugs,

as a pre-treatment or prophylactic," Dr Lenz said.

"They would remain in circulation and be capable of destroying toxic, xenobiotic materials in the bloodstream before they could do any harm. So we have an interest in paraoxonase from that aspect."

3D advance

Joel Sussman, Israel Silman, Dan Tawfik and colleagues at the Weizmann Institute in Rehovot, Israel, outlined recently the structure of the paraoxonase Pon1 at the first international conference on the paraoxonases in Ann Arbor, US. The structure was determined using the technique of X-ray crystallography.

"Having the 3D structure puts us in a position where we can begin to see how to modify some of the groups in the active site and test if they could work effectively against the more toxic nerve agents," Professor Sussman told BBC News Online.

The researchers believe drugs based on the molecules could eventually be made available to the public.

A paraoxonase prophylactic might work on the same principle as enzyme replacement therapy, used to treat a disorder of the metabolism called Gaucher's disease.

The enzyme could be administered by injection and would remain in the blood for hours or days.

Public control

But the principle of unsupervised use of anti-nerve agent drugs by civilians concerns some experts.

"When people are given things to self-administer they will often overdose in anticipation of an attack," said Dr Sally Lievesley, of UK-based security consultant New Risk.

"You have to have something that's not highly toxic. Under an extreme weapons attack the dose that soldiers have may produce side effects but it's going to keep them alive. You're dealing with a disciplined group.

"But there are different criteria if you're dealing with peacetime populations who may self-dose ahead of time. With the general public you're into a different level of safety."

But Dr Lievesley added that it was not uncommon for military products to have civilian spin-offs.

Insulin experience

"I can't see why it would be different from any other medicine," Professor Silman explained.

"The most difficult thing with all these things is that they have to be compatible with the immune system. But there's nothing impossible about this."

He pointed out that insulin, which could be lethal in overdose, was routinely self-administered by diabetics.

Dr Lievesley said there was a race on to develop prophylactic drugs for use by those in the emergency services who might have to respond to multiple attacks with chemical weapons.

"The difficulty with nerve agents is their rapidity of action," Professor Alistair Hay, a chemical weapons specialist at the University of Leeds, UK, said.

"Organophosphate nerve agents are very fast acting through inhalation. But you might have more leeway with skin penetration.

"You have to have a reasonable residence time in the blood for them to be efficacious. What you need to do is prevent exposure in the first place with good masks, good protective suits and that's where the emphasis needs to be."

Story from BBC NEWS:
<http://news.bbc.co.uk/go/pr/fr/-/2/hi/science/nature/3671827.stm>

Published: 2004/05/02 23:35:09 GMT

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